

Název: Interaction study of selected amino acids with
platinum cytostatics

Školitel: Natalia Cernei

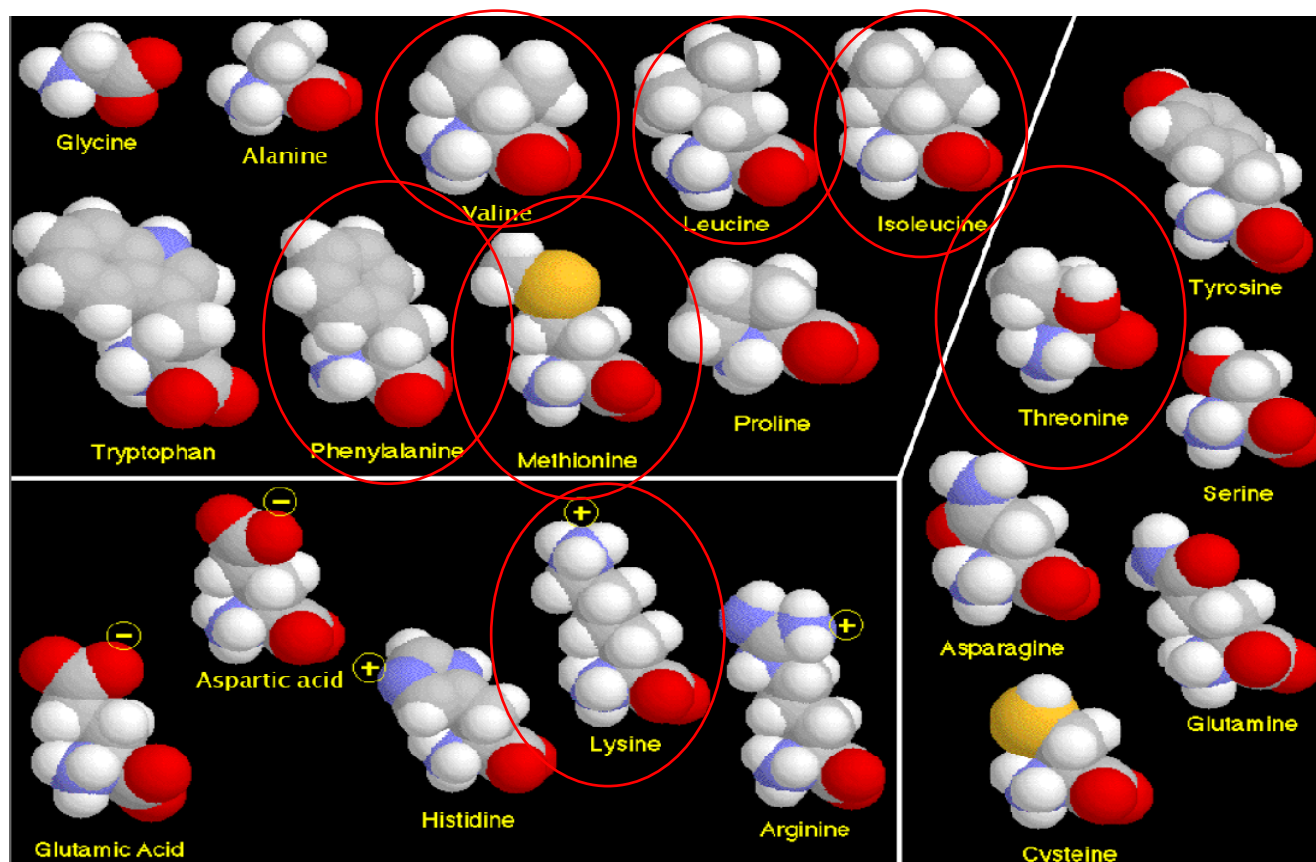
Datum: 31.10.2014

Reg.č.projektu: CZ.1.07/2.3.00/20.0148

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



INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

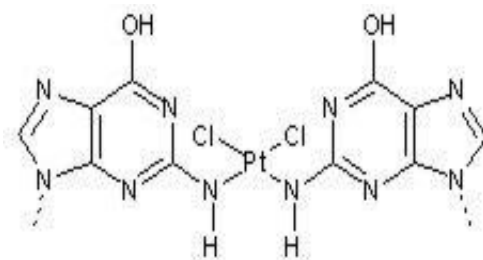
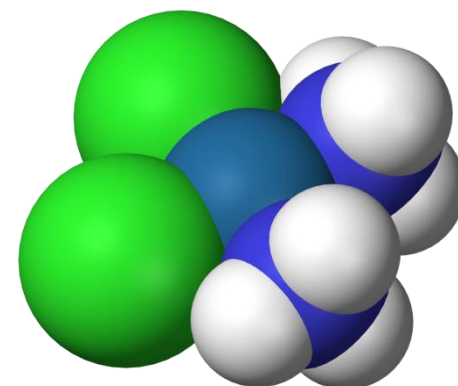


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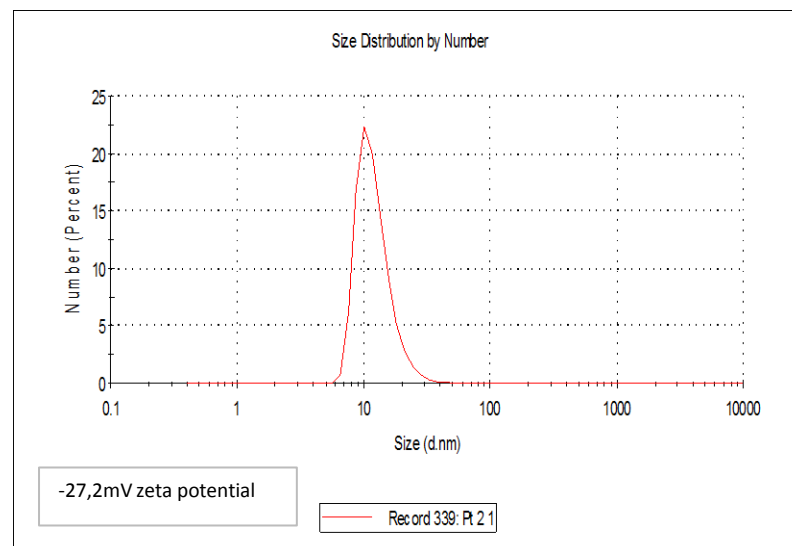
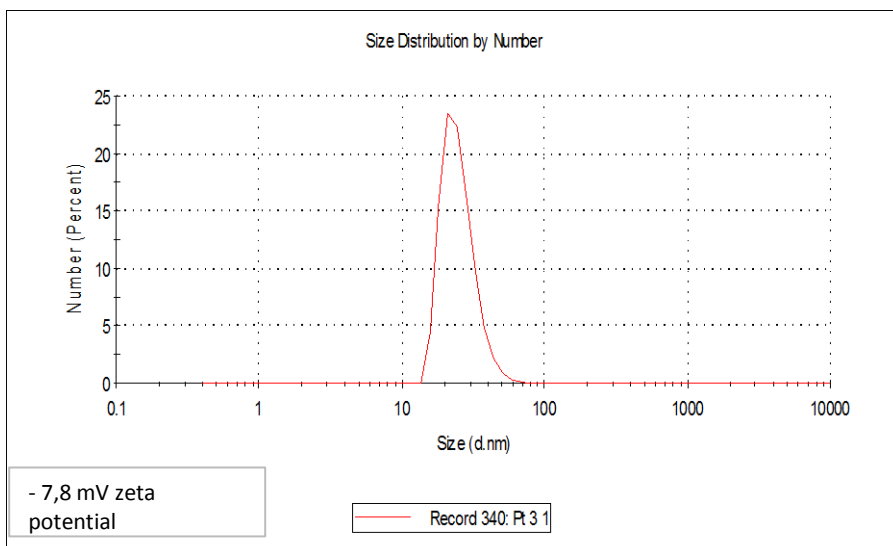
The compound $cis\text{-}[\text{Pt}(\text{NH}_3)_2(\text{Cl})_2]$ was first described by Michele Peyrone in 1845, and known for a long time as Peyrone's salt. Cis $\text{PtCl}_2(\text{NH}_3)_2$ was indeed highly effective at regressing the mass of sarcomas in rats. Confirmation of this discovery, and extension of testing to other tumour cell lines launched the medicinal applications of cisplatin. Cisplatin was approved for use in testicular and ovarian cancers by the U.S. Food and Drug Administration on 19 December 1978. Cisplatin combination chemotherapy is the cornerstone of treatment of many cancers. Used to treat testicular, ovarian, bladder, head and neck, esophageal, small and non-small cell lung, breast, stomach and prostate cancers, neuroblastoma, sarcomas, melanoma. It has a significant emetogenic effect, reducing kidney function hydration, may reduce blood formation.



Platinum (Pt) is a noble metal with unique physiological and chemical properties widely used in chemistry, physics, biology, and medicine. Regarding the biological activities of Pt, it is known that Pt compounds have the ability to arrest the cell cycle and cause DNA strand breaks. The DNA damage is caused by Pt ions, which attach to N7 sites of DNA guanine bases and, after hydrolysis of Pt-Cl bonds, form adducts with the DNA double helix. These properties of Pt are exploited in cancer therapy in the form of antineoplastic drugs to treat different types of cancer such as head, neck, brain, testicular, bladder, ovarian, or uterine cervix carcinomas. However, toxic side effects of Pt-based drugs are major drawbacks in cancer therapy. Platinum nanoparticles (NP-Pt) have recently elicited much interest because of their physicochemical properties such as catalytic activity and high reactivity.



Malvern Zetasizer (NANO-ZS, Malvern Instruments Ltd., Worcestershire, U.K.)



Pt 3: PVP Polyvinylpyrrolidone 10.000 (MW),
(C₆H₉NO)_n

Pt 2: PVP Polyvinylpyrrolidone
40.000(MW), (C₆H₉NO)_n

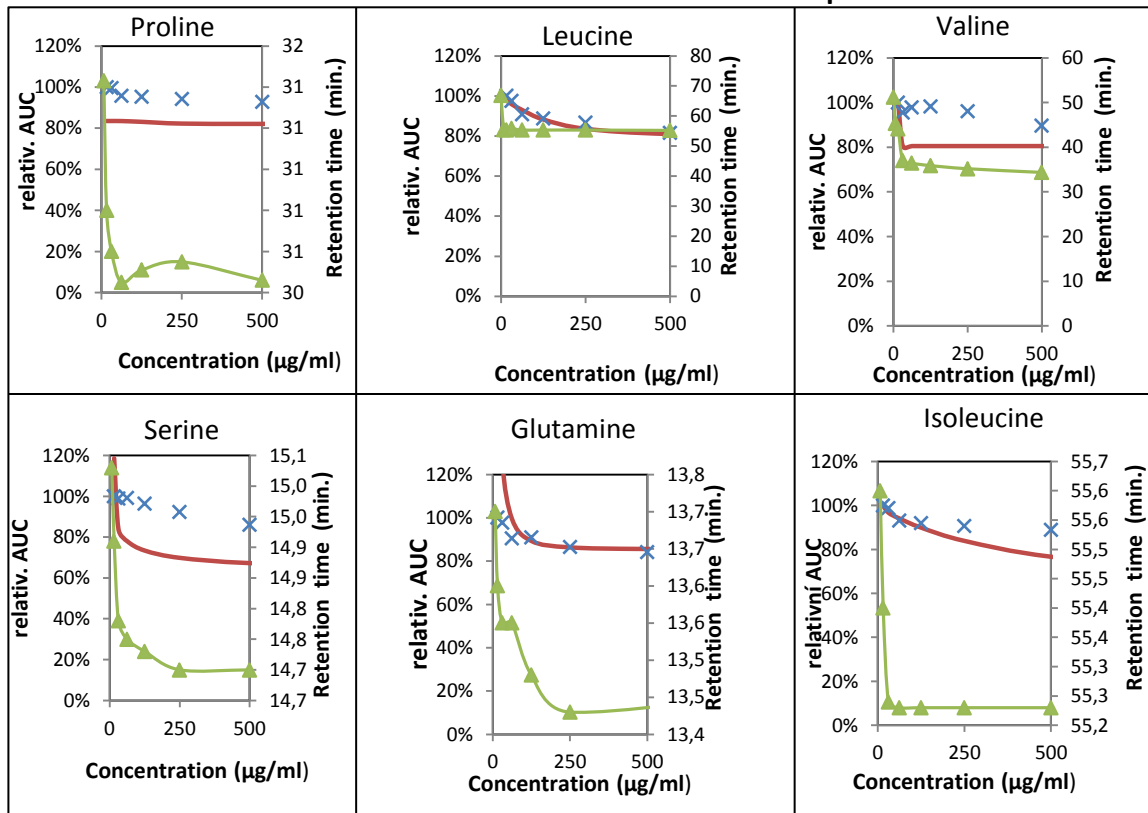
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INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

Addition of cisplatin



500 µg/ml
250 µg/ml
125 µg/ml
62 µg/ml
31 µg/ml
15,6 µg/ml
7µg/ml
0

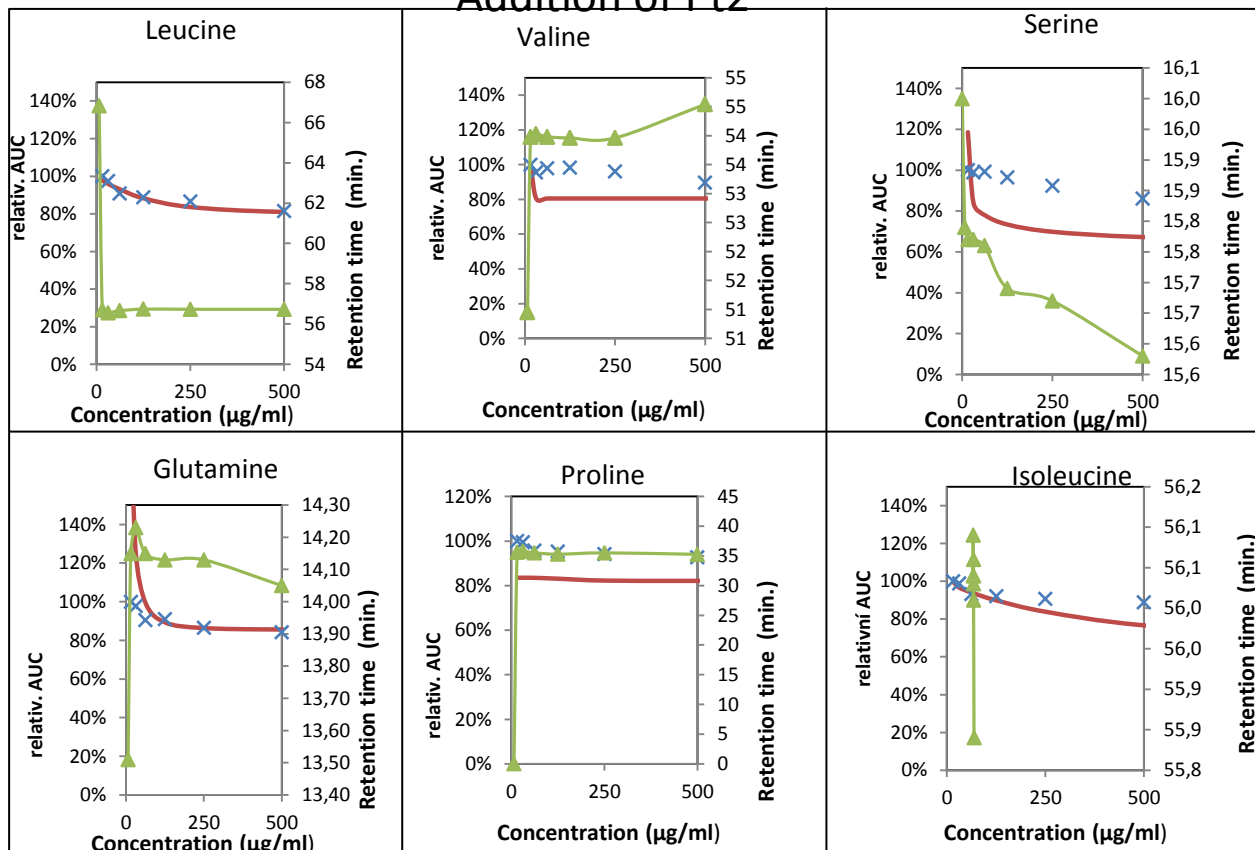
Cisplatin
Pt2
Pt3

X Sample
— calculated overlay expressing amino acids breaking points.
▲ Expression of retention time changes (min)



INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

Addition of Pt2



500 µg/ml
250 µg/ml
125 µg/ml
62 µg/ml
31 µg/ml
15,6 µg/ml
7µg/ml
0

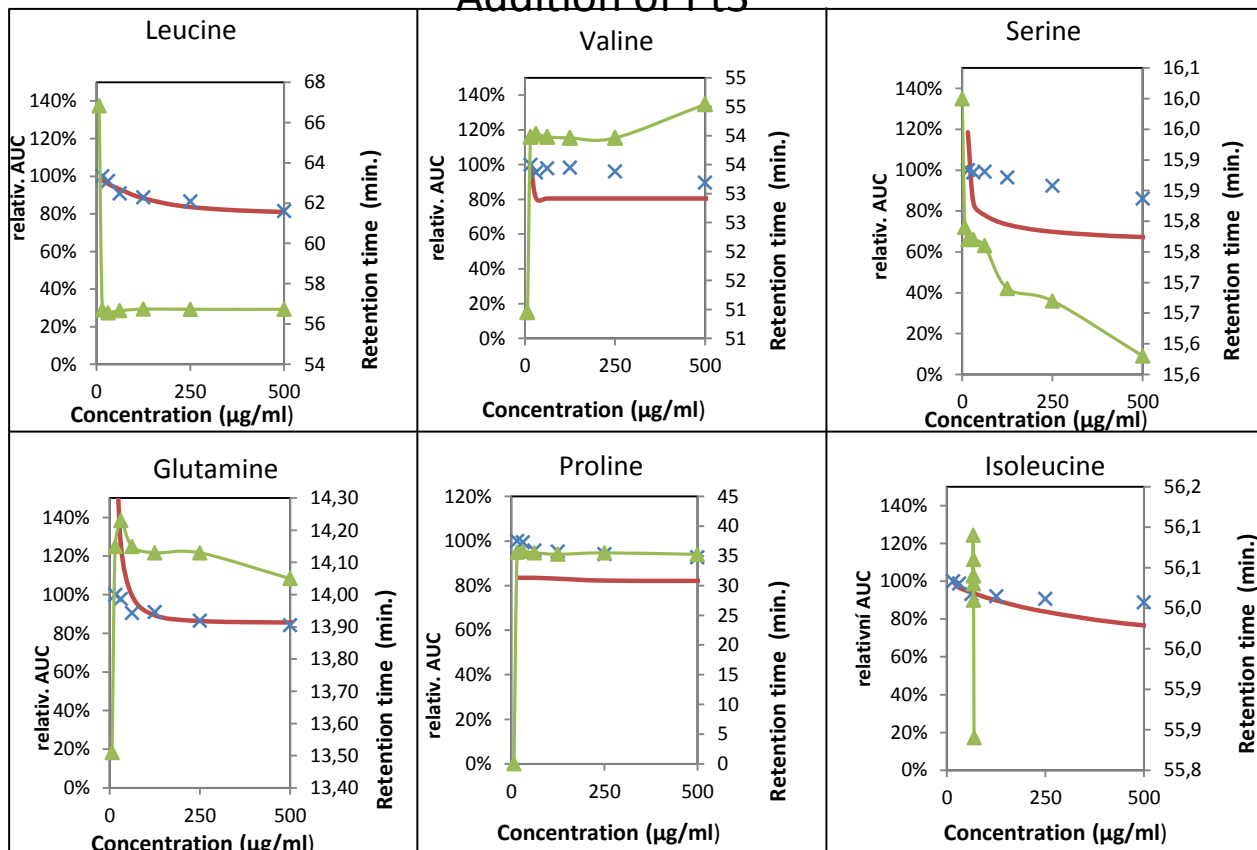
Cisplatin
Pt2
Pt3

X Sample
—calculated overlay
expressing amino acids
breaking points.
▲ Expression of retention
time changes (min)



INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

Addition of Pt3



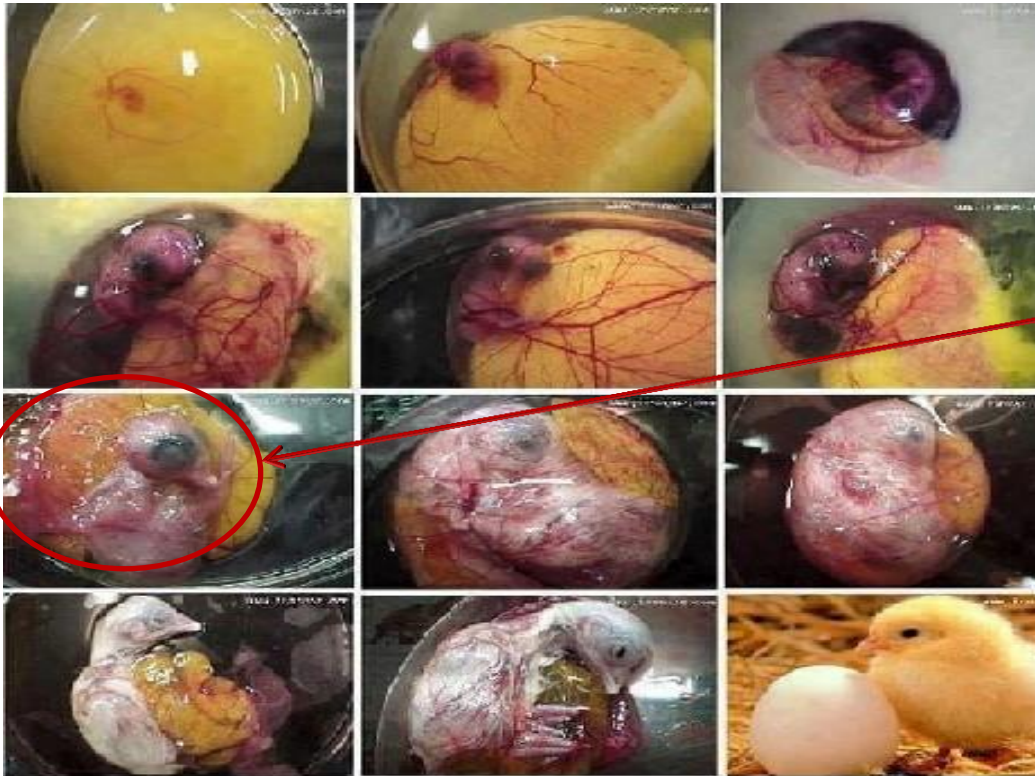
500 µg/ml
250 µg/ml
125 µg/ml
62 µg/ml
31 µg/ml
15,6 µg/ml
7µg/ml
0

Cisplatin
Pt2
Pt3

X Sample
— calculated overlay expressing amino acids breaking points.
▲ Expression of retention time changes (min)



INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ



15 µg/ml
7,5 µg/ml
3,75 µg/ml
1,9 µg/ml
0

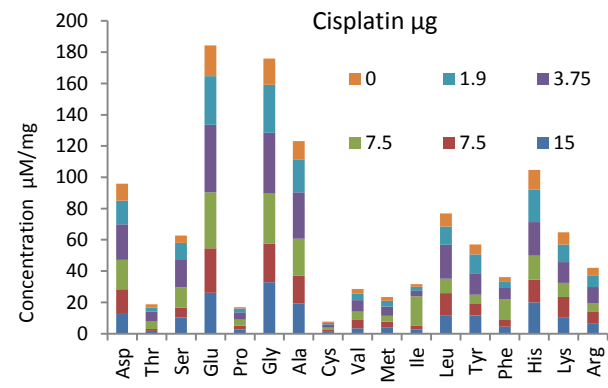
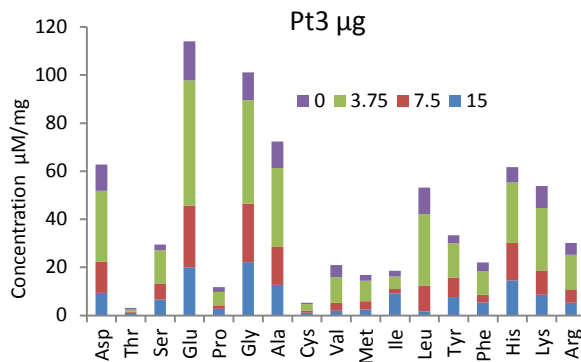
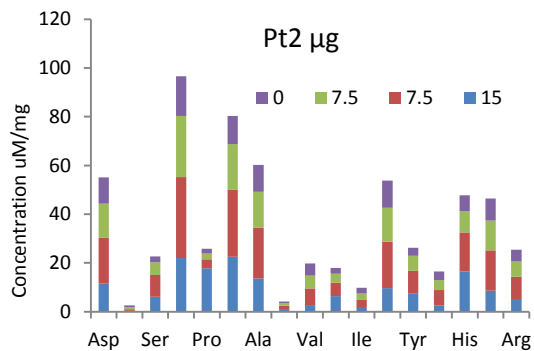
Cisplatin
Pt2
Pt3

The development of a chicken, from fertilization to hatching. The process takes around 21 days.

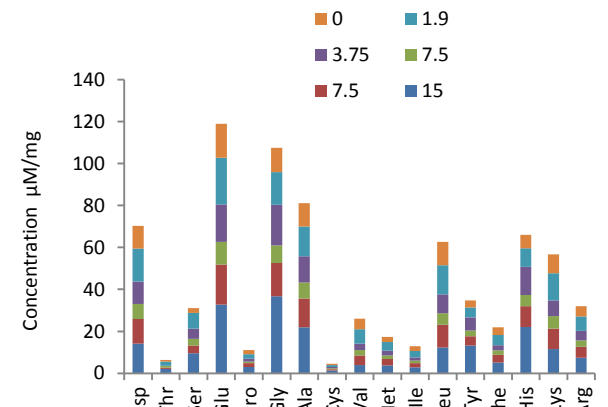
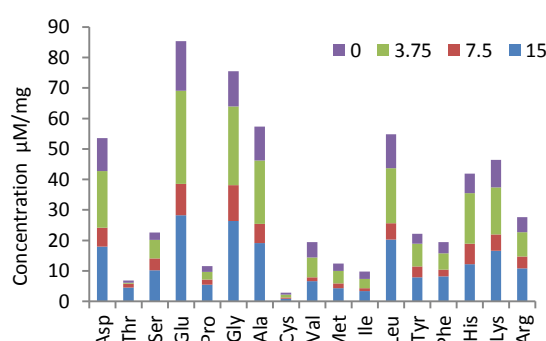
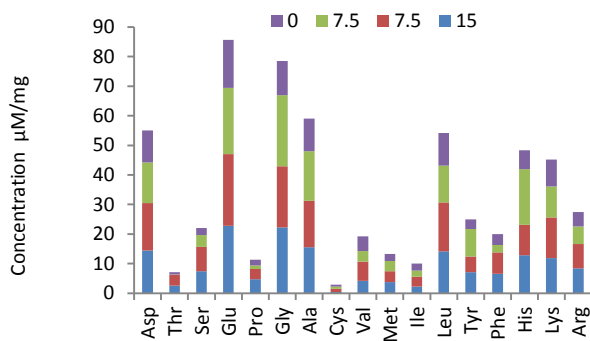


INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

Embryos chicken kidney



Embryos chicken liver



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Conclusion

An effect of cytostatics on amino acids may be an important factor involved in this multifactorial and very complicated process. Possible formations of complexes may play important role in the adverse effects of cytostatics; however, this phenomenon must be further investigated. Cisplatin chemotherapy is also associated with cardiotoxic effects that may range from silent arrhythmias to heart failure and even sudden cardiac death. Understanding the pathophysiology of cardiac dysfunction associated with cytostatics is important for prediction, treatment, and prevention of these adverse side effects of chemotherapy. From these purposes we have the future plans to carry out *in vivo* experiments, further uncovering this phenomenon.

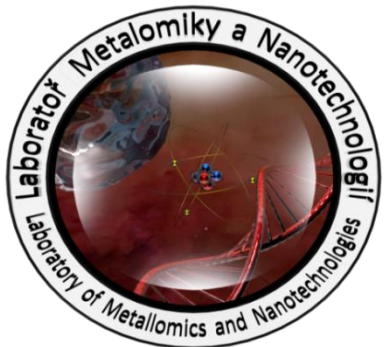
Acknowledgment



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Thank you for your attention!



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OP Vzdělávání
pro konkurenceschopnost

INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

Mendel
University
in Brno

