Doctoral Conference

Microfluidic Systems For Drug Analytical Applications

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Introduction

Cancer

- 10 million deaths per year [1]
- 19 million newly diagnosed cancer patients [1]
- The leading cause of death worldwide
- The 5-year survival of the most common cancers is still low

Chemotherapy (CT)

- Widely used to treat malignancies
- 60%-of all cancer patients ~11 million people were treated
- CT protocols are established on a **"one size fits all"** basis

Ignore inter-patient differences in drug pharmacokinetic

Leading to improper dosing
Drug resistance and **unwanted side effects**

Therapeutic Drug Monitoring (TDM) is the key to improve and personalize CT

- The lack of an affordable point-of-care (POC) method
- Mass Spectrometry is the „golden standard"
- No TDM- capable device

TDM is a non-existing strategy in clinical oncology

Concept

The aim is to prove that TDM can be implemented in cancer therapy.

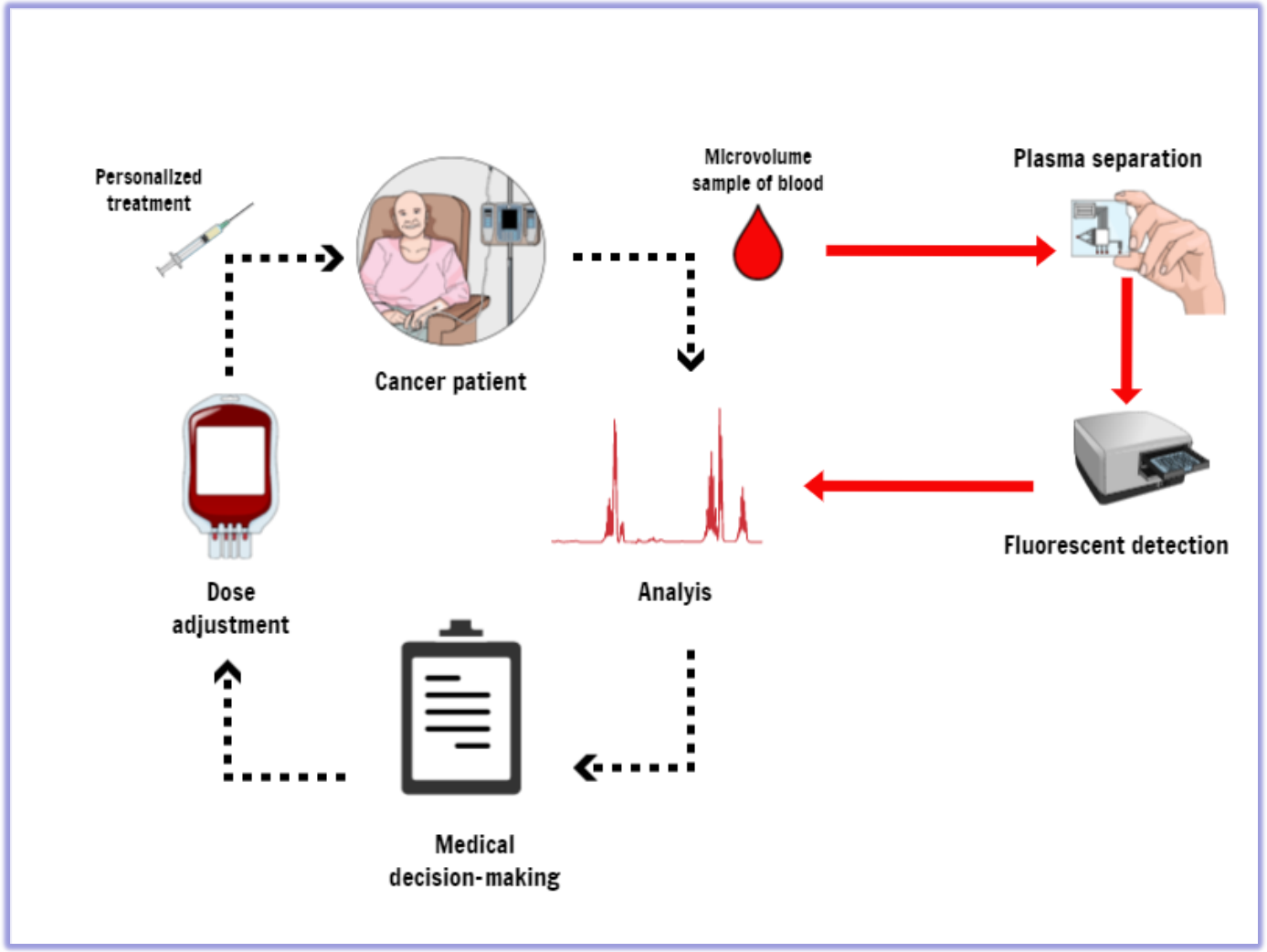
The most important information for successful cancer treatment

⇩

Blood concentration levels of the anticancer drug

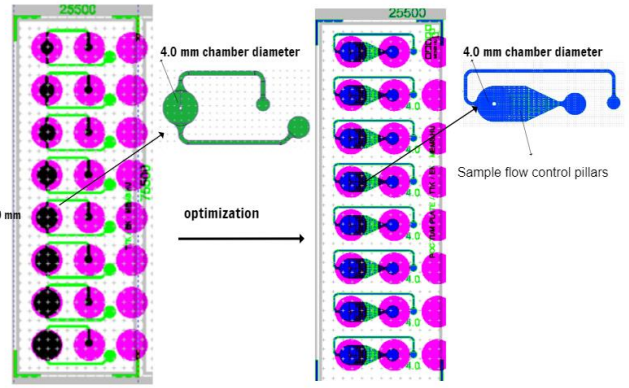
TDM- capable microfluidics-based blood sample analysis device

1. „Drop of blood”
2. Microfluidic Chip – blood separation
3. Microfluidic Chip – plasma collection
4. Fluorescent measurement
5. Personalized treatment

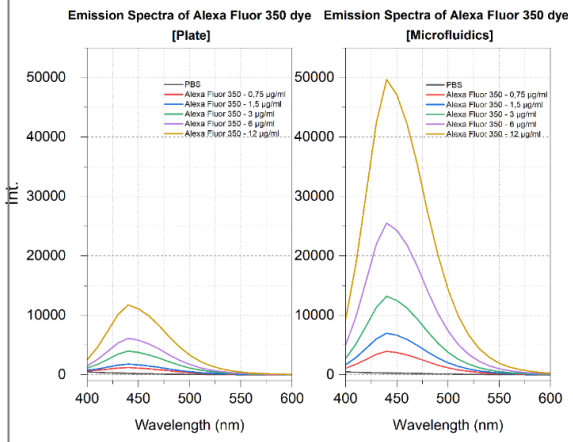


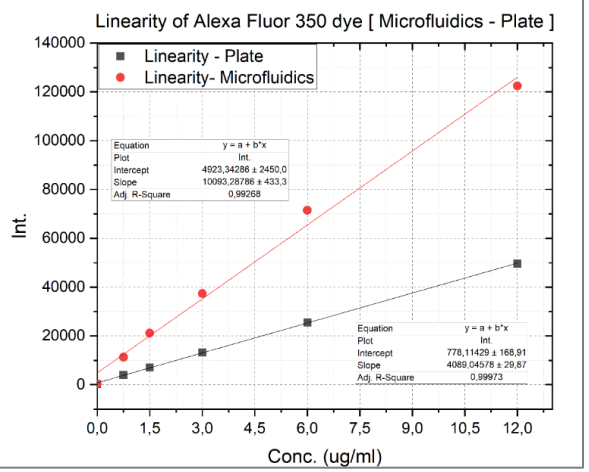
Results in the previous semesters

1. Microfluidics – device development

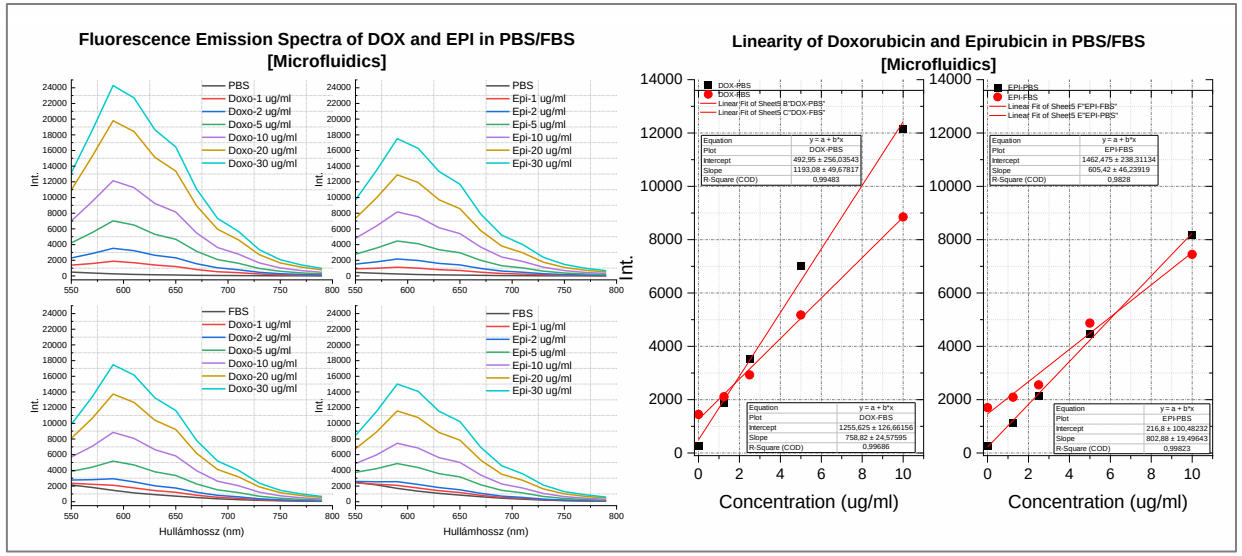


2. Fluorescent method development





3. Fluorescent method development for Anthracyclines



Conclusions

- ✓ The microfluidic chip is suitable for the detection of microvolume samples
- ✓ Suitable for measuring the concentration of chemotherapeutic drugs having fluorescent properties (Anthracyclines)

1. Detection method for Doxil

Anthracyclines – Doxil

- Encapsulated- Liposomal doxorubicin
- Widely used group of chemotherapeutics- childhood cancer/breast cancer/lymphomas
- Fluorescent emission at 600 nm - detection in biological samples

Advantages

- Significant increase in both relapse-free and overall survival
- Delayed onset of drug resistance

Disadvantages

- Light scattering on nanoparticles

- Additional sample preparation is required
- Precipitation of liposomes is required

Method development

- The spectral properties of Doxil were screened by using Tecan Spark in a conventional plate and a microfluidic chip
- Absorption and fluorescence emission spectra were determined for detailed spectral properties
- The effect of using different solvents (PBS, FBS, acetonitrile - ACN) on the signal intensity was characterized
- The effect of ACN treatment on liposomes precipitation and the signal intensity was analysed
- The effect of volume reduction on signal intensity was tested in a microfluidic environment
- Signal intensity and linearity were tested in a microfluidic environment

Detection Method

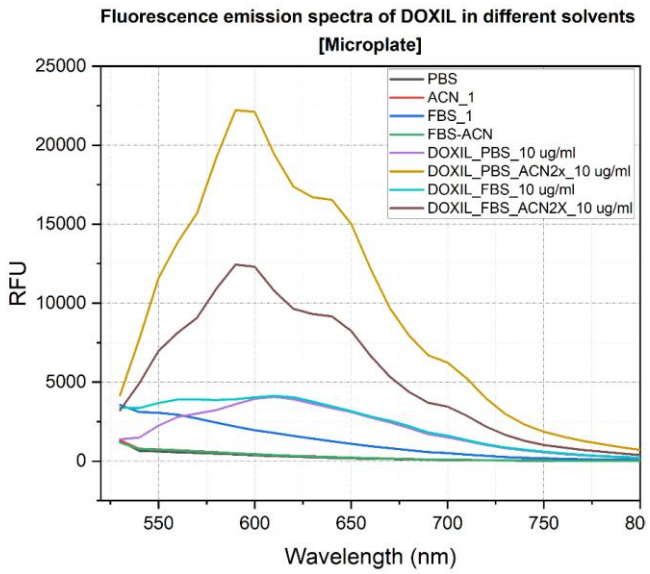
Fluorescent emission spectra of Doxil were screened in microplate and microfluidics in different solvents (PBS, FBS, ACN)

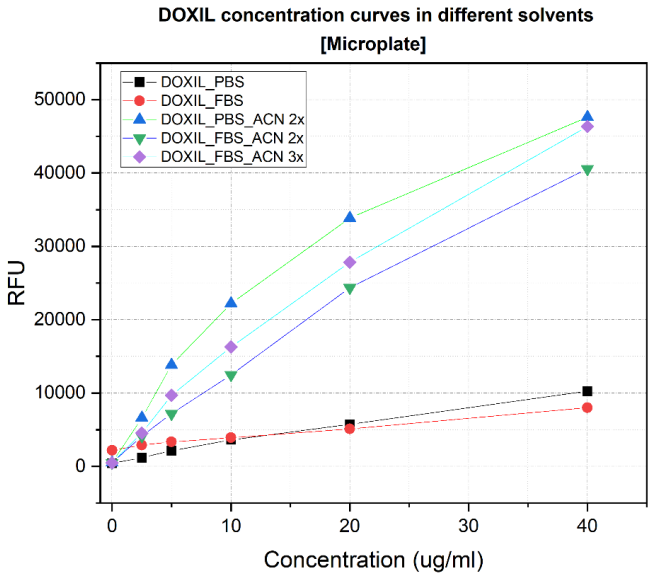
The signal intensity and linearity were tested in a microfluidic environment

Treatment of ACN increased the signal intensity

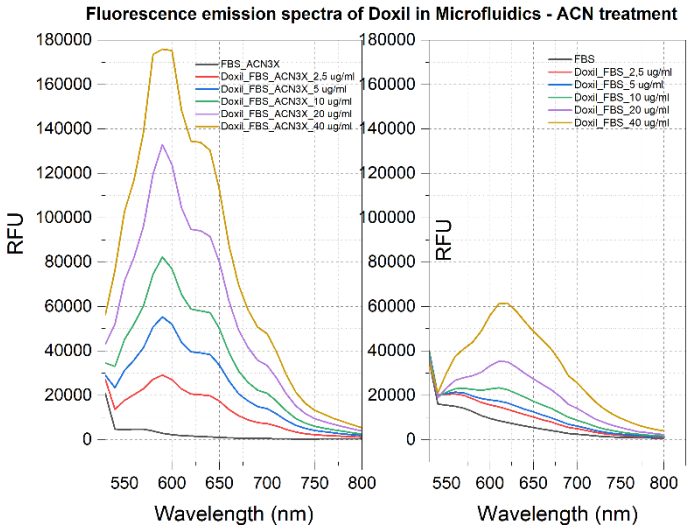
- Precipitation of liposomes
- Precipitation of peptides from FBS
- Solvent polarity affected the signal intensity

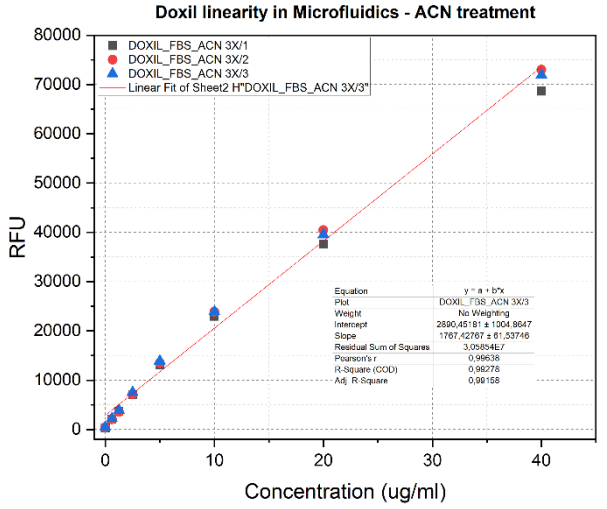
1. Results in microplate





2. Results in microfluidics





Results in the 3rd semester

Fluorescence drugs screening

- Systemic screening for fluorescent drugs
- Determine the spectral properties of a wide library of commercially available chemotherapeutic drugs used to treat leukemia
- Identify the molecules with fluorescent characteristics

84 different chemotherapeutic drugs from Servier were screened by Tecan Plate Reader

- More than 20 drugs showed intense fluorescence emission in the visible spectral range
- potential characteristics to be applied for the selective detection of these molecules even in biological samples

Conclusions

- ✓ The microfluidic chip is suitable for the detection of microvolume samples
- ✓ Suitable for measuring the concentration of chemotherapeutic drugs having fluorescent properties (Anthracyclines)

- ✓ Doxil was proved to be able to detect
- ✓ 84 different chemotherapeutic drugs from Servier were screened - cca. 25% showed intense fluorescence emission in the visible spectral range

Future plans

1. To validate the TDM microfluidics with blood samples from different animal models and to compare the results to MS.

2. To design and manufacture a microfluidic chip which able to passively separate plasma from micro volumes of whole blood.

3. To individualize chemotherapy treatments using TDM in animal models

Publications

1. Bereczki, Haffaressas, Fürjes, Füredi „**Optical parameters of leukemia-related chemotherapeutic drugs**” Congress of the International Association of Therapeutic Drug Monitoring & Clinical Toxicology (IATDMCT), Sept 24-27, 2023, Oslo, Norway (accepted)

2. Füredi, Bereczki, Gombos, Haffaressas, Szabó, Vajdovich, Fürjes **"Point-of-Care Therapeutic Drug Monitoring of chemotherapy from microvolume blood samples with a specifically designed microfluidic system**” Congress of the International Association of Therapeutic Drug Monitoring & Clinical Toxicology (IATDMCT), Sept 24-27, 2023, Oslo, Norway (accepted)

Subjects

1. **Nanotechnology** – chemical materials science (Éva Kiss)

2. **Transmission electron microscopy** for structural investigations of different materials (Katalin Balázsi)

Thanks for your attention!