

# Spatiotemporal imaging and pharmacokinetics of fluorescent compounds in zebrafish eleuthero embryos after different routes of administration

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## Organisation

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## SCOPE OF THE METHOD

<b>The Method relates to</b>	Other: Different routes of administration in zebrafish eleuthero embryos
<b>The Method is situated in</b>	Translational - Applied Research
<b>Type of method</b>	In vivo
<b>Used species</b>	Zebrafish
<b>Targeted organ system or type of research</b>	General pharmacokinetics

## DESCRIPTION

### Method keywords

zebrafish embryo

Spatiotemporal imaging

### **Scientific area keywords**

pharmacokinetics

exposure routes

### **Method description**

The spatiotemporal distribution of fluorescent compounds was examined during 48 h after immersion (10  $\mu$ M) or microinjection (2 mg/kg) in the pericardial cavity (PC), intraperitoneally (IP) and yolk sac (IY) of 3 dpf zebrafish eleuthero-embryos. By modelling the fluorescence of whole-body contours present in fluorescence images, the main pharmacokinetic (PK) parameter values of the compounds were determined. It was demonstrated that especially in case of short incubations (1–3 h) immersion can result in limited intrabody exposure to compounds. In this case, PC and IP microinjections represent excellent alternatives. Significantly, IY microinjections did not result in a suitable intrabody distribution of the compounds. Performing a QSPkR (quantitative structure-pharmacokinetic relationship) analysis, LogD was identified as the only molecular descriptor that explains the final uptake of the selected compounds. It was also shown that combined administration of compounds (immersion and microinjection) provides a more stable intrabody exposure, at least in case of a prolonged immersion and compounds with LogD value > 1.

### **Lab equipment**

- Microinjector,
- Fluorescent stereomicroscope.

### **Method status**

Published in peer reviewed journal

## **PROS, CONS & FUTURE POTENTIAL**

### **Advantages**

Taken together, the data show that the immersion route can result in limited

intrabody exposure to compounds, especially in case of short incubations (typically 1–3 h), possibly resulting in false-negative results in screening programs. The results of this method will help reduce the risk of false negative results and can offer an invaluable input for future translational research and safety assessment applications.

## Challenges

Considering that often thousands of compounds are tested in ZF drug screens, performing injections of compounds does not always seem feasible. Based on the results obtained in this study we recommend to employ prolonged incubation times (e.g. 24 h), at least in case compounds exhibit LogD values below 1. Alternatively, if not toxic to the eleuthero-embryos, higher concentrations than 10  $\mu$ M can be used as well, although in the present study the relationship between immersion concentrations and relative uptake was not studied, and no final conclusions on this matter can be given.

## REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

### References

<https://doi.org/10.1038/s41598-021-91612-6>

### Associated documents

[Spatiotemporal imaging and pharmacokinetics of fluorescent compounds in zebrafish eleuthero-embryos after different routes of administration.pdf](#)

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