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

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SCOPE OF THE METHOD

The Method relates to	Other: Different routes of administration in zebrafish eleuthero embryos
The Method is situated in	Translational - Applied Research
Type of method	In vivo
Used species	Zebrafish
Targeted organ system or type of research	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 μM) or microinjection (2 mg/kg) in the pericardial cavity (PC), intraperitoneally (IP) and yolk sac (IY) of 3 dpf zebrafsh 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 identifed 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 µM 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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