Electronic supplementary information

Metallomics for drug development: a further insight into intracellular activation chemistry of a ruthenium(III)-based anticancer drug gained by multidimensional analytical approach†

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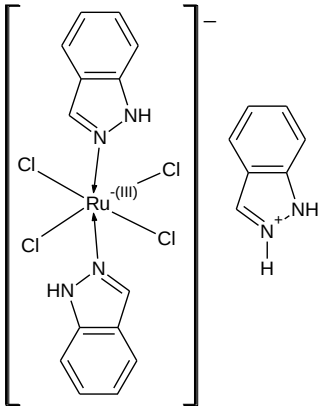

Scheme S1. Structural formula of the Ru drug.

Table S1. CE, ICP-MS, and ESI-MS/MS settings and operational parameters

Parameter	Setting
ICP-MS	
plasma gas flow rate, L min^{-1}	15
auxiliary gas flow rate, L min^{-1}	0.9
sample cone	Pt (1.0 mm orifice)
skimmer cone	Pt (0.4 mm orifice)
plasma RF power, W	1290
isotopes monitored	^{100}Ru, ^{101}Ru, ^{102}Ru, ^{57}Fe, ^{72}Ge, ^{89}Y
dwell time, ms	100
Interface	
spray chamber volume, mL	5
nebulizer gas flow rate, L min^{-1}	1.0
CE	

Capillary	fused-silica, inner diameter 75 μm, length 70 cm (50 cm effective length)
Background electrolyte	10 mM NaH_2PO_4–10 mM Na_2HPO_4, 4 mM NaCl, pH 6.0
sample injection, mbar×s	300
voltage, kV	25
current, μA	28–30
sheath liquid	1 mM phosphate buffer (pH 6.0), 0.4 mM NaCl, 20 μg L^{-1} Ge
ESI-MS/MS	
syringe pump speed, μL min^{-1}	18
polarity	positive (+), negative (-)
mode	SCAN, Product Ion
mass range, m/z	50–1500
ionization voltage, V	2500 (+), 1500 (-)
orifice voltage, V	90
drying gas flow, L min^{-1}	8
drying gas temperature, °C	300
nebulizer pressure, psi	50
sheath gas flow, L min^{-1}	7
sheath gas temperature, °C	350
nozzle voltage, V	500
collision energy, eV	20 or 30

Conditions for capillary pretreatment

Prior to analysis, the capillary was conditioned with 0.1 M NaOH (10 min), a mixture of 0.1 M NaOH, methanol, and water (25/50/25, v/v/v) (5 min), water (5 min), and background electrolyte (10 min). After each analysis, the capillary was rinsed with the same solutions and in the same sequence for 1, 1, 1, and 3 min, respectively (with a 0.5 min pause between flushes). After flushing, the stability of the current (29±1 µA) was checked by applying a constant voltage of 25 kV for 30 s. The electrolyte was degassed in the ultrasonic bath and passed through a 0.45 μm membrane filter before analysis.

Measurement of EOF

The EOF was measured by means of UV-detected acetone (Fig. S1). Preliminary experiments carried out with and without the EOF marker indicated that the addition of a small amount of acetone to the incubation mixture before the CE run does not virtually affect the peak area and migration time of the adduct (variations below 3%). This allowed us to neglect possible denaturation effects.

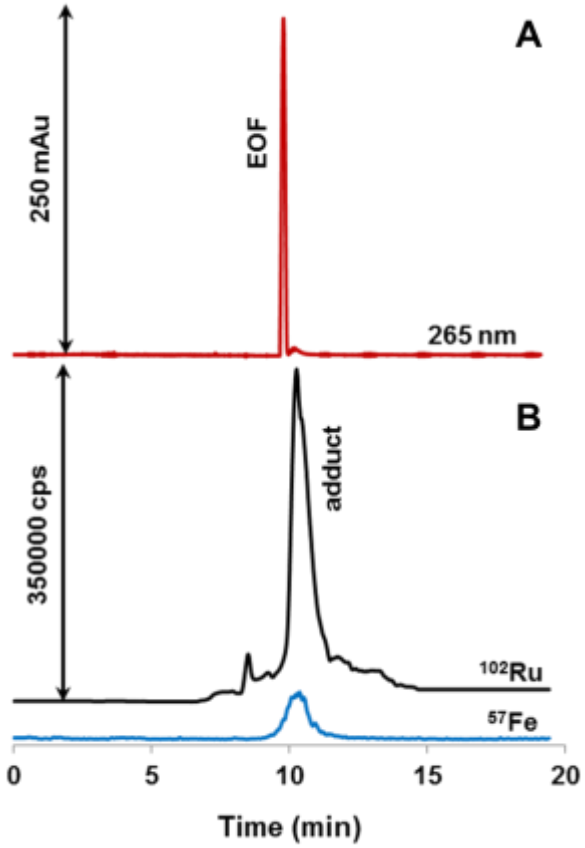

Figure S1 Comparison between the rate of EOF (A) and the mobility of Ru–transferrin adduct (5×10^{-5} M).

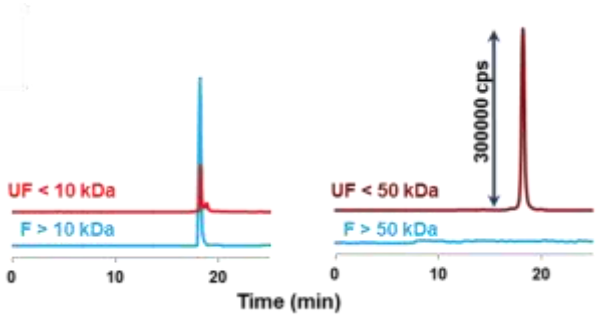

Figure S2 Electropherograms profiling the effect of glutathione on the Ru distribution between LMM (UF) and HMM (F) fractions (both after 24 h of incubation).