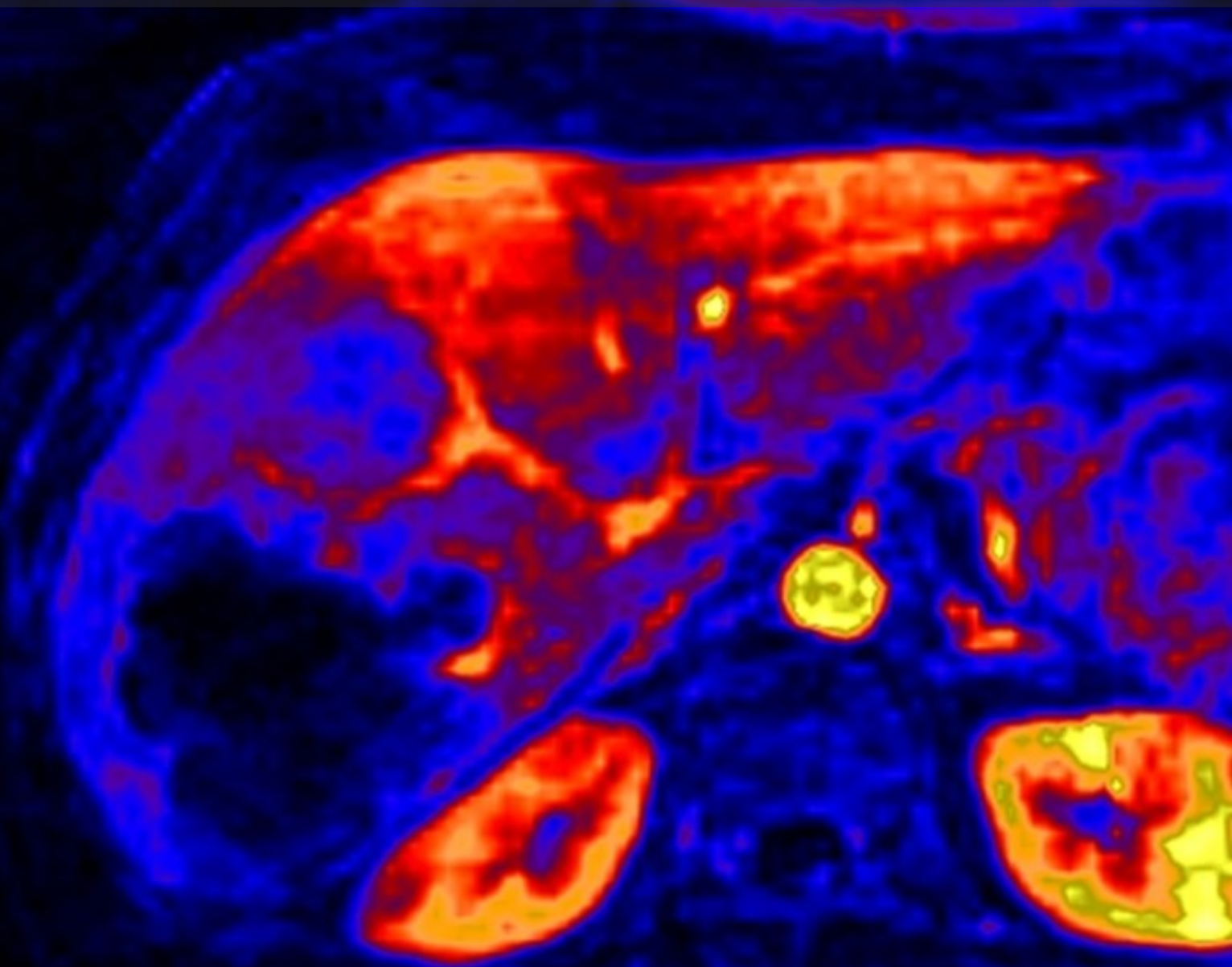


# Sheffield two-compound study

metformin (key results)

D2.13 - Internal report

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metformin (key results)

by

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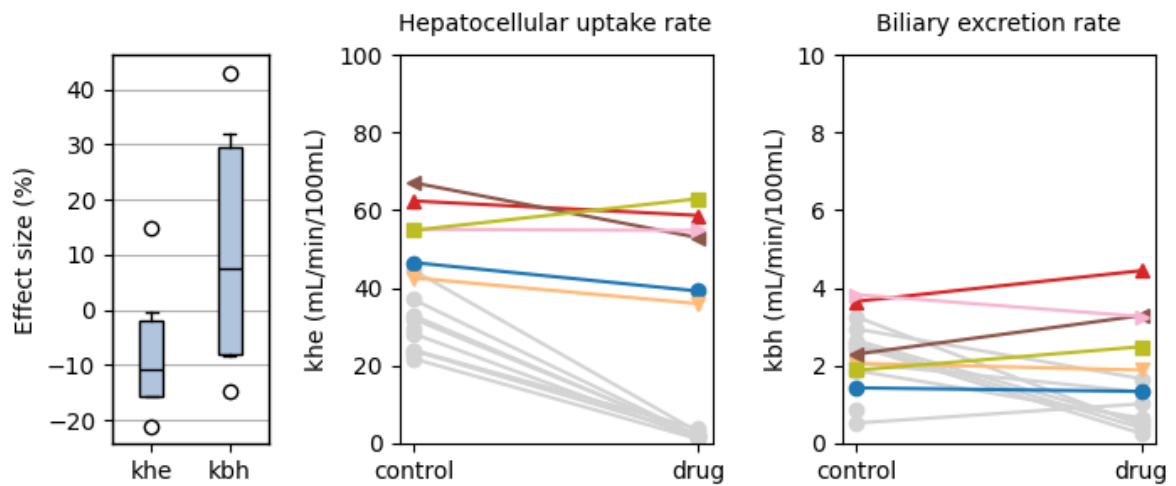


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# Key results

## 1.1. Data summary



**Figure 1.1:** Effect size (%) on hepatocellular uptake ( $k_{he}$ , left) and biliary excretion ( $k_{bh}$ , right) of gadoxetate. The boxplot shows median, interquartile range and 95 percent range. The line plots show individual values for hepatocellular uptake ( $k_{he}$ , middle) and biliary excretion ( $k_{bh}$ , right) of gadoxetate of the control (left of plot) and treatment (right of plot). Grey lines are healthy controls with rifampicin injection.

	parameter	count	mean	std	min	25%	50%	75%	max
	khe effect size (%)	6.0	-7.3	13.2	-21.0	-15.7	-10.8	-1.9	14.9
	khe control (mL/min/100cm <sup>3</sup> )	6.0	54.74	9.22	42.6	48.59	54.94	60.55	67.06
	khe drug (mL/min/100cm <sup>3</sup> )	6.0	50.74	10.81	35.96	42.64	53.86	57.68	62.94
	kbh effect size (%)	6.0	11.2	24.2	-14.7	-8.0	7.6	29.5	43.1
	kbh control (mL/min/100cm <sup>3</sup> )	6.0	2.53	0.98	1.43	1.93	2.18	3.32	3.83
	kbh drug (mL/min/100cm <sup>3</sup> )	6.0	2.78	1.12	1.34	2.04	2.88	3.28	4.44

**Table 1.1:** Effect size and absolute values of hepatocellular uptake ( $k_{he}$ ) and biliary excretion ( $k_{bh}$ ) of gadoxetate

## 1.2. Liver biomarkers

Biomarker	p-value	Bayes Factor	Odds Ratio
AUC for CI (0-35min)	0.76793	0.39	0.77
AUC for CI (0-inf)	0.95528	0.37	1.06
Biliary excretion rate	0.35326	0.56	0.64
Biliary tissue excretion rate	0.7676	0.39	1.17
Extracellular dispersion	0.23017	0.72	4.19
Extracellular mean transit time	0.47682	0.47	2.41
Final biliary excretion rate	0.26405	0.66	0.45
Final hepatocellular uptake rate	0.68796	0.4	1.44
Hematocrit			
Hepatocellular mean transit time	0.83026	0.38	0.9
Hepatocellular tissue uptake rate	0.26673	0.66	0.28
Hepatocellular uptake rate	0.24898	0.69	2.06
Initial biliary excretion rate	0.8499	0.38	1.11
Initial hepatocellular uptake rate	0.59543	0.42	1.71
Liver T1-MOLLI at 45min	0.49899	0.46	0.65
Liver T1-MOLLI at baseline	0.46924	0.48	1.92
Liver T1-MOLLI at scan 2	0.37867	0.53	3.57
Liver blood clearance	0.22127	0.74	1.78
Liver extracellular volume fraction	0.05543	1.94	10.6
RE for R1l at 20min	0.88785	0.38	0.89
RE for Sl at 20min	0.63696	0.41	0.69

**Table 1.2:** Results of a pairwise comparison testing for differences in liver biomarkers between control and treatment. The results are ranked by their p-value, with most significant differences at the top of the list.

Biomarker	Units	control	drug	change (%)
AUC for CI (0-35min)	mM*sec	192.0 (48.0)	199.0 (29.0)	14.3 (35.0)
AUC for CI (0-inf)	mM*sec	681.0 (310.0)	671.0 (120.0)	47.4 (89.0)
Biliary excretion rate	mL/min/100cm3	2.53 (0.79)	2.78 (0.89)	11.2 (19.0)
Biliary tissue excretion rate	mL/min/100cm3	3.35 (0.98)	3.25 (0.84)	-0.0278 (19.0)
Extracellular dispersion	%	74.9 (4.2)	62.5 (17.0)	-16.1 (24.0)
Extracellular mean transit time	sec	23.8 (2.6)	20.0 (8.4)	-12.6 (41.0)
Final biliary excretion rate	mL/min/100cm3	2.22 (0.54)	2.62 (0.88)	16.6 (24.0)
Final hepatocellular uptake rate	mL/min/100cm3	62.2 (22.0)	57.9 (11.0)	1.59 (24.0)
Hematocrit	%	45.0 (0.0)	45.0 (0.0)	0.0 (0.0)
Hepatocellular mean transit time	min	33.3 (9.3)	34.0 (9.7)	4.63 (19.0)
Hepatocellular tissue uptake rate	mL/min/100cm3	223.0 (43.0)	598.0 (600.0)	156.0 (240.0)
Hepatocellular uptake rate	mL/min/100cm3	54.7 (7.4)	50.7 (8.6)	-7.34 (11.0)
Initial biliary excretion rate	mL/min/100cm3	3.07 (1.4)	2.99 (0.93)	6.3 (29.0)
Initial hepatocellular uptake rate	mL/min/100cm3	47.3 (12.0)	43.6 (6.8)	4.37 (42.0)
Liver T1-MOLLI at 45min	sec	0.445 (0.062)	0.47 (0.098)	5.58 (13.0)
Liver T1-MOLLI at baseline	sec	0.761 (0.025)	0.75 (0.023)	-1.31 (3.5)
Liver T1-MOLLI at scan 2	sec	0.621 (0.076)	0.568 (0.041)	-5.77 (18.0)
Liver blood clearance	L/min	0.538 (0.11)	0.49 (0.14)	-10.4 (12.0)
Liver extracellular volume fraction	mL/100cm3	25.1 (2.6)	16.1 (7.4)	-36.3 (27.0)
RE for R1l at 20min	%	72.0 (24.0)	73.4 (10.0)	27.3 (61.0)
RE for Sl at 20min	%	61.7 (21.0)	65.8 (9.4)	36.2 (70.0)

**Table 1.3:** Mean values along with their 95 percent confidence intervals for all liver biomarkers of the control and treatment visit. The last column shows the relative change at the treatment visit. The results are ranked by their p-value, with most significant differences at the top of the list.

### 1.3. Systemic biomarkers

Biomarker	p-value	Bayes Factor	Odds Ratio
AUC for Cb (0-35min)	0.31911	0.59	0.4
AUC for Cb (0-inf)	0.74479	0.39	0.7
Body extraction fraction	0.81785	0.38	1.36
Cardiac output	0.2283	0.73	1.53
Heart-lung dispersion	0.38416	0.53	2.74
Heart-lung mean transit time	0.93329	0.37	1.11
Organs blood mean transit time	0.3065	0.6	2.09
Organs extraction fraction	0.08979	1.37	0.28
Organs extravascular mean transit time	0.04821	2.14	8.42
RE for R1b at 20min	0.56233	0.44	0.58
RE for Sb at 20min	0.89265	0.38	1.15

**Table 1.4:** Results of a pairwise comparison testing for differences in systemic biomarkers between control and treatment visit. The results are ranked by their p-value, with most significant differences at the top of the list.

Biomarker	Units	control	drug	change (%)
AUC for Cb (0-35min)	mM*sec	23.6 (6.0)	27.3 (5.9)	26.0 (40.0)
AUC for Cb (0-inf)	mM*sec	44.4 (19.0)	48.5 (13.0)	46.0 (83.0)
Body extraction fraction	%	5.44 (2.2)	5.05 (1.2)	19.4 (54.0)
Cardiac output	L/min	10.5 (3.5)	9.49 (3.2)	-9.24 (15.0)
Heart-lung dispersion	%	57.1 (14.0)	48.9 (8.4)	-8.09 (23.0)
Heart-lung mean transit time	sec	15.0 (4.2)	14.8 (3.7)	9.95 (46.0)
Organs blood mean transit time	sec	32.8 (9.8)	28.1 (8.4)	-10.2 (30.0)
Organs extraction fraction	%	17.2 (2.1)	19.1 (2.3)	11.8 (11.0)
Organs extravascular mean transit time	min	8.02 (0.89)	6.93 (0.57)	-12.6 (9.5)
RE for R1b at 20min	%	14.2 (4.5)	15.7 (3.4)	29.5 (56.0)
RE for Sb at 20min	%	13.2 (5.1)	12.8 (3.9)	20.5 (67.0)

**Table 1.5:** Mean values along with their 95 percent confidence intervals for all systemic biomarkers at the control and treatment visit. The last column shows the relative change at the treatment visit. The results are ranked by their p-value, with most significant differences at the top of the list.