SUPPLEMENTARY DATA

Hepatobiliary events in migraine therapy with herbs – The case of Petadolex, a Petasites hybridus extract

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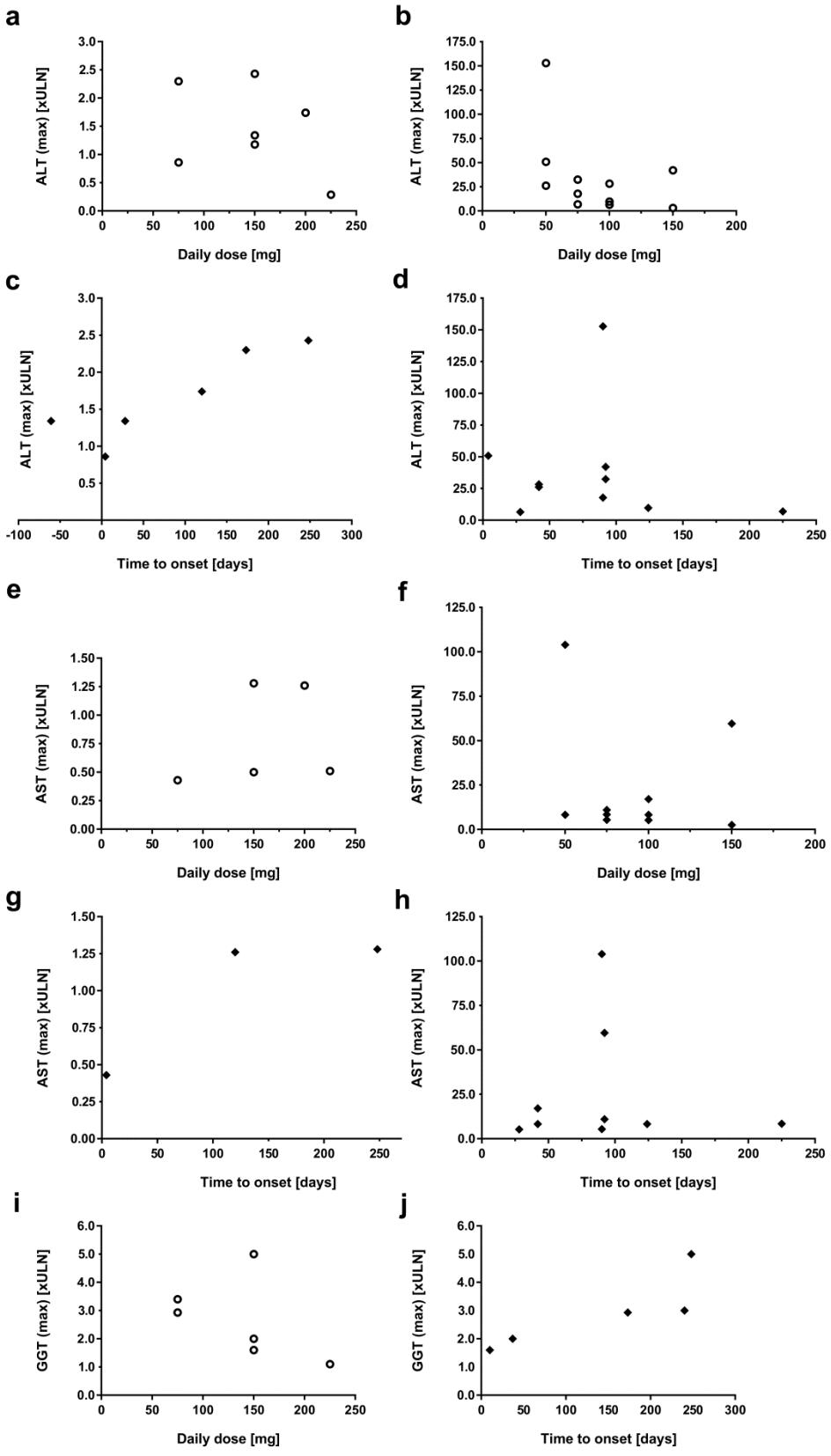
Supplementary Figure S1. Serum biochemistry changes (ALT, AST, GGT) in regards to dose and time to onset of HILI.



Panel A: ALT in relation to dose ≤ 3x ULN

Panel B: ALT in relation to dose > 3x ULN

Panel C: ALT in relation to time to onset ≤ 3x ULN

Panel D: ALT in relation to time to onset > 3x ULN

Panel E: AST in relation to dose ≤ 3x ULN

Panel F: AST in relation to dose > 3x ULN

Panel G: AST in relation to time to onset ≤ 3x ULN

Panel H: AST in relation to time to onset > 3x ULN

Panel I: GGT in relation to dose

Panel J: GGT in relation to time to onset

Supplementary Table S1: Information on individual human donors, which donated liver tissue for the generation of human hepatocyte cultures.

Donor ID	Sex	Age	Diagnosis
1	Male	67	Klatskin Tumor
2	Male	74	Liver metastasis of colorectal carcinoma
3	Male	69	Liver metastasis of colorectal carcinoma
4	Male	57	Liver metastasis of colorectal carcinoma
5	Female	77	Liver metastasis of ovarian tumor
6	Male	57	Liver metastasis of colorectal carcinoma
7	Male	36	Liver metastasis of colorectal carcinoma
8	Female	41	Liver metastasis of ovarian tumor
9	Male	50	Liver metastasis of colorectal carcinoma

Supplementary Table S2: Clinical biochemistry data and major histopathology findings after repeated oral dosing of rats with a Petasites hybridus extract for 6 months.

Study group	**Vehicle control**		**45mg/kg**		**135 mg/kg**		**270 mg/kg**	
gender	**M**	**F**	**M**	**F**	**M**	**F**	**M**	**F**
Serum biochemistry								
AST*	30.05 (±1.52)	32.60 (±2.47)	32.30 (±2.80)	29.50 (±4.06)	29.40 (±1.06)	27.10 (±1.15)	26.48 (±5.46)	25.88 (±3.15)
Bilirubin*	1.81 (±0.59)	2.03 (±0.43)	2.04 (±0.86)	2.13 (±0.74)	2.48 (±0.97)	2.15 (±0.92)	3.35 (±1.74)	2.13 (±0.76)
ALAT*	18.23 (±1.65)	15.58 (±2.89)	20.09 (±0.95)	19.17 (±5.73)	20.40 (±2.10)	16.60 (±2.38)	15.43 (±.1.71)	13.13 (±1.23)
GGT *	0.68 (±0.53)	0.68 (±0.61)	1.03 (±0.78)	0.77 (±0.15)	1.13 (±0.25)	0.83 (±0.55)	2.10 (±1.66)	2.85 (±2.15)
AP *	162.78 ±82.07	111.23 ±53.88	180.10 ±87.04	87.87 ±47.33	179.43 ±84.68	93.20 ±43.68	156.70 ±83.40	89.35 ±41.81
Histological findings								
Focal lymphocytosis ** (number of animals)	0	2	4	4	5	4	1	3
Bile duct hyperplasia** (number of animals)	0	0	0	0	10	5	17	13
Bile duct dilatation** (number of animals)	0	0	0	0	0	0	16	3
Minimal lipidosis** (number of animals)	7	4	5	4	4	3	9	6

* 4 animals per dose and gender; data are units per liter
** 20 animals per dose and gender; data are individual animals with a histological finding