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(54) Benævnelse: **Medical use of sPLA2 hydrolysable liposomes**

(57) Sammendrag:

The present invention relates to medical use of liposomes, more particular the first medical use of sPLA2 hydrolysable liposomes. Such liposomes may be used for targeted delivery of therapeutic agents to cancerous tissue and in such embodiments; the therapeutic agents are typically small molecule antitumor agents. Other aspects of the inventions relates to methods of reducing the side effects of therapeutic agents, e.g. reducing nephrotoxicity, neurotoxicity and gastrointestinal toxicity of a therapeutic agent. Yet another aspect of the present invention relate to methods of prolonging the therapeutic effect of a therapeutic agent.

fortsættes

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Efficacy of liposomal cisplatin. MT-3 breast xenografts

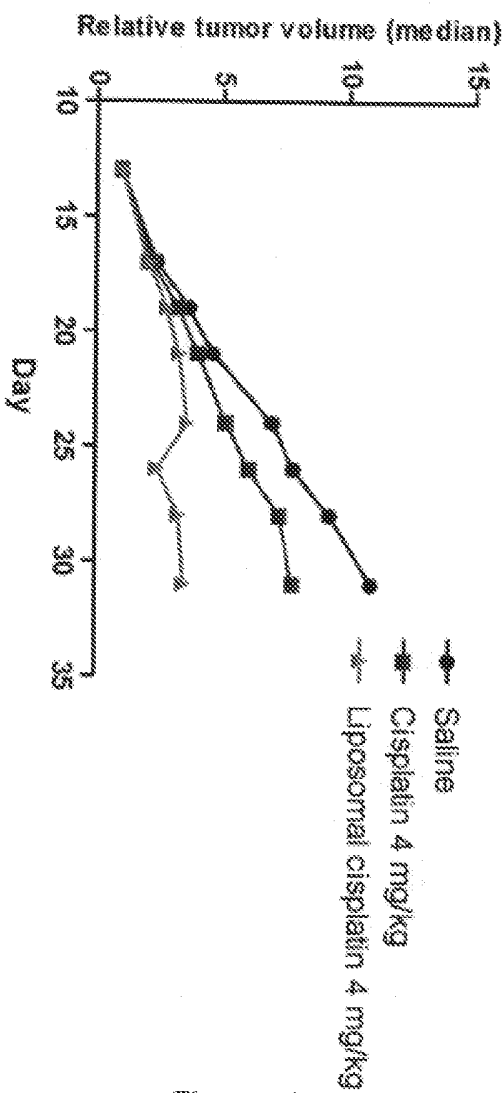


Figure 1

Claims

- 1) A sPLA2 hydrolysable liposome for use in therapy.
- 5 2) The liposome of claim 1, wherein the content of anionic lipid is between 20% and 45%, the content of polymer conjugated lipid is between 3% and 6% and the content of neutral lipids is between 40% and 75%.
- 10 3) The liposome of claim 2, wherein the anionic lipid is DSPG, the neutral lipid is DSPC and the polymer conjugated lipid is DSPE-PEG.
- 15 4) The liposome of any of the preceding claims, wherein the liposome is administered intravenous administration in form of bolus injection or infusion.
- 20 5) The liposome of any of the preceding claims, wherein the liposome comprises a therapeutic agent.
- 25 6) The liposome of any of the preceding claims, wherein the therapeutic agent is a small molecule antitumour agent is selected from the group consisting of: anthracyclin derivatives, cisplatin, oxaliplatin, carboplatin, picoplatin, doxorubicin, paclitaxel, 5-fluoruracil, exisulind, cis-retinoic acid, suldinac sulphide, methotrexate, bleomycin and vincristine.
- 30 7) The liposome of any of the preceding claims, wherein the small molecule antitumor agent is a platinum based antitumor agent selected from the group consisting of cisplatin, oxaliplatin, picoplatin and carboplatin.
- 8) The liposome of any of the preceding claims, wherein the dose of the therapeutic agent is reduced as compared to the standard dose of the free therapeutic agent.
- 9) The liposome of any of the preceding claims, wherein the dose of the therapeutic agent is increased as compared to the standard dose of the free therapeutic agent.

10) The liposome of any of the preceding claims, wherein liposome is administered at prolonged intervals as compared to the standard dosing regimen of the free compound.

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Efficacy of liposomal cisplatin. MT-3 breast xenografts

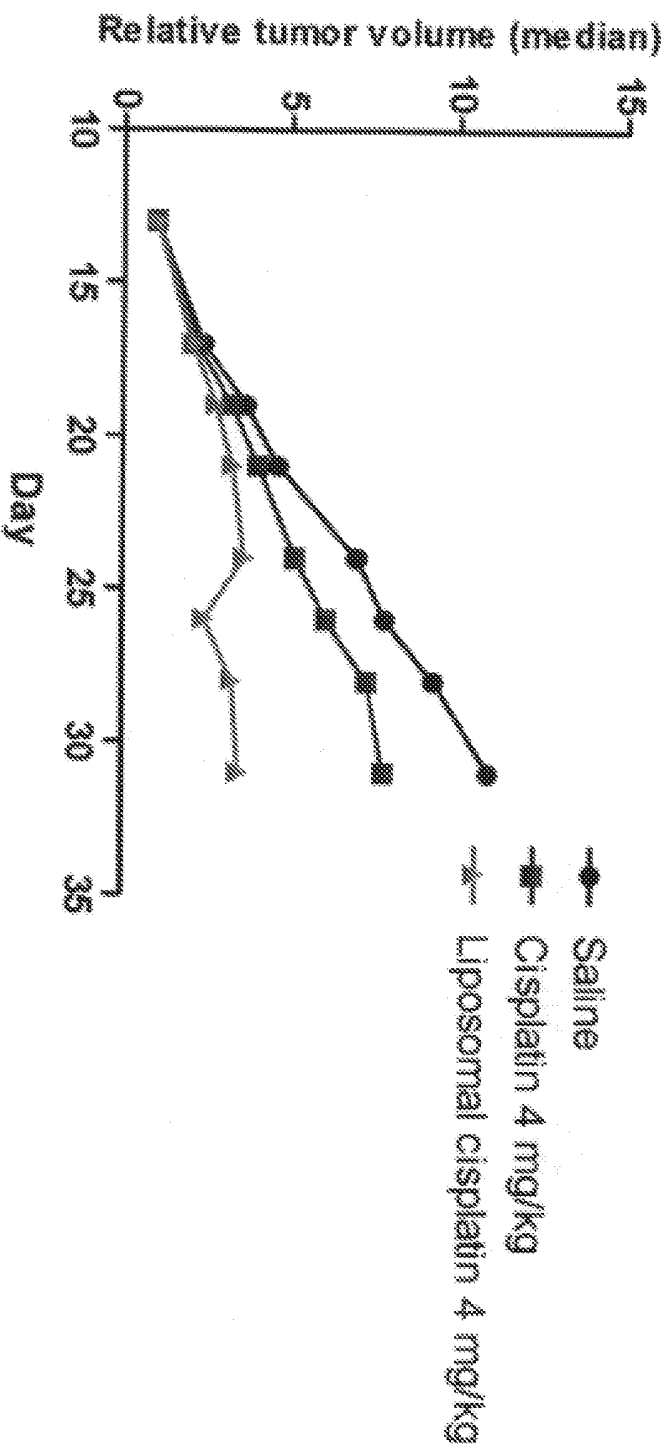


Figure 1

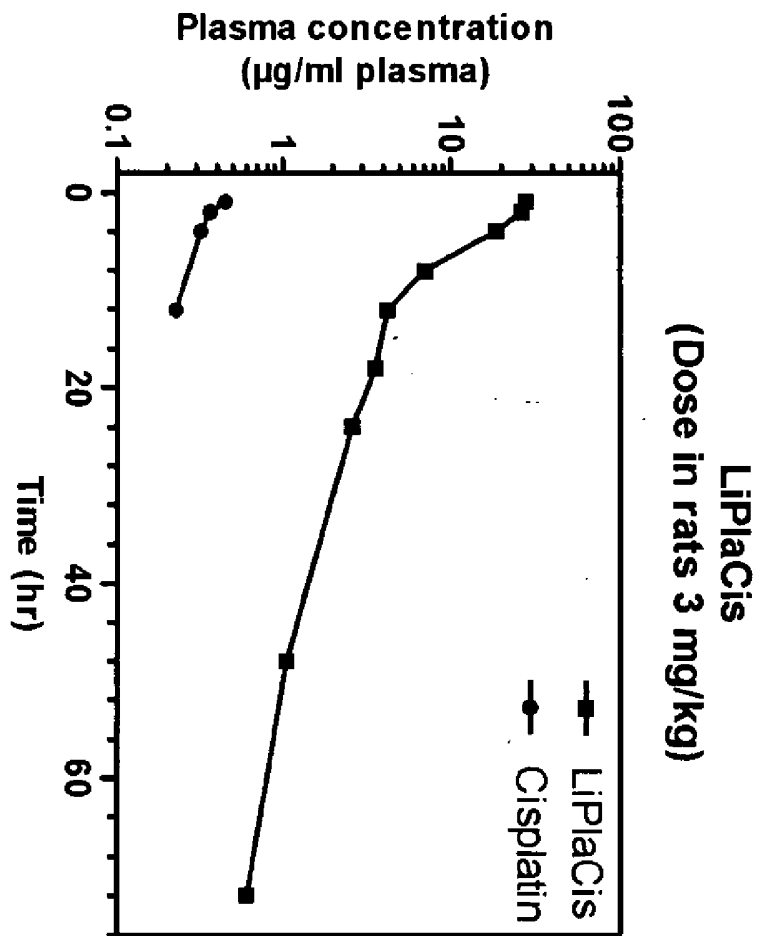


Figure 2

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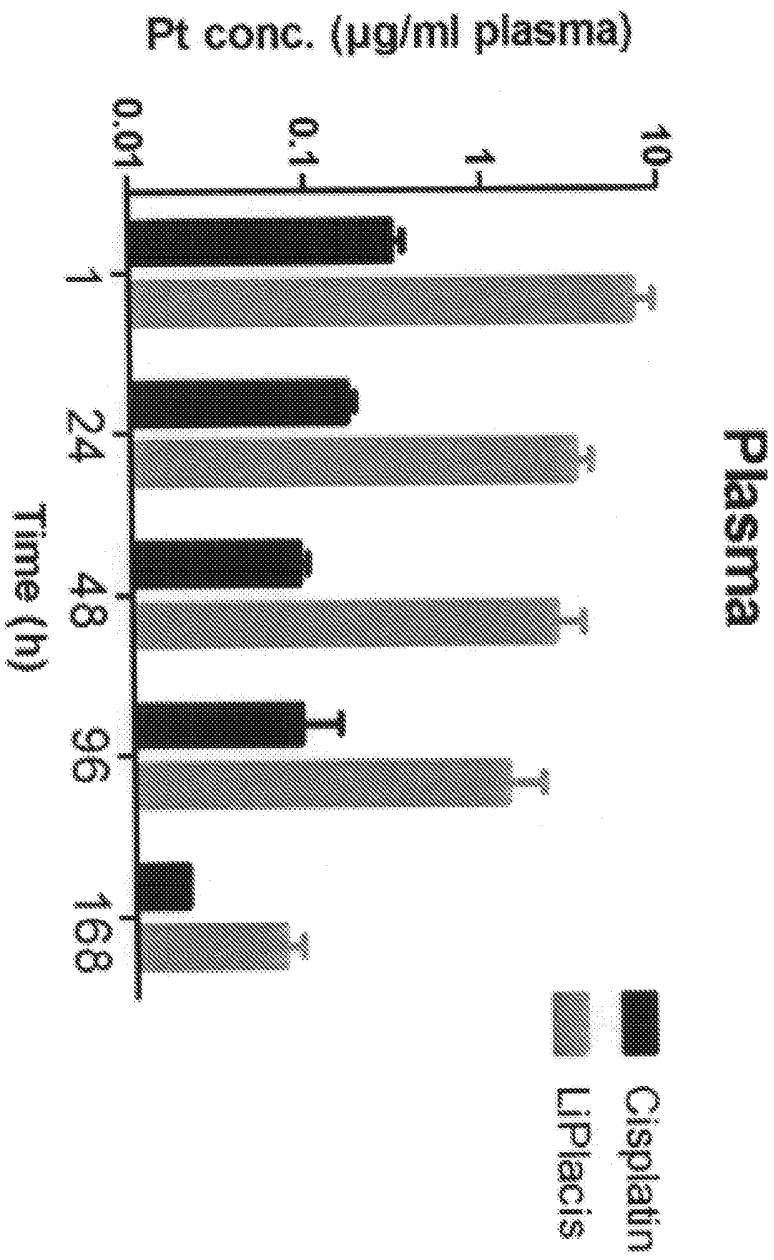


Figure 3

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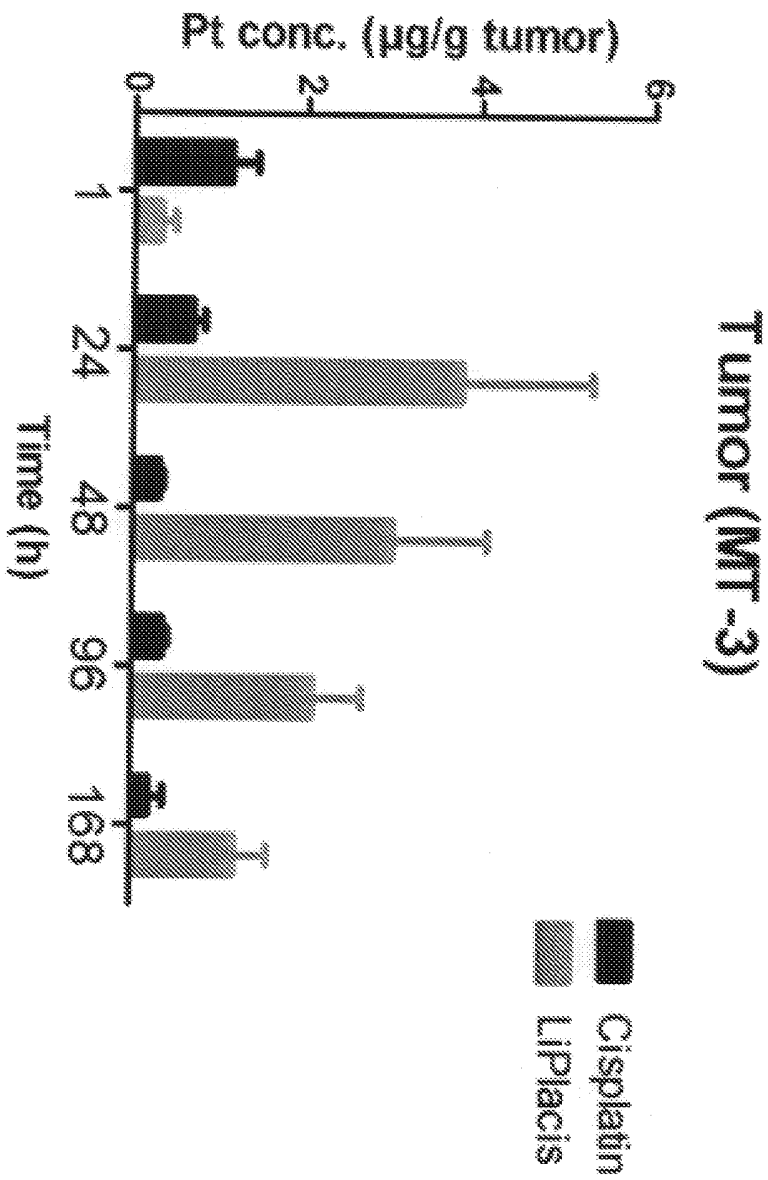


Figure 4

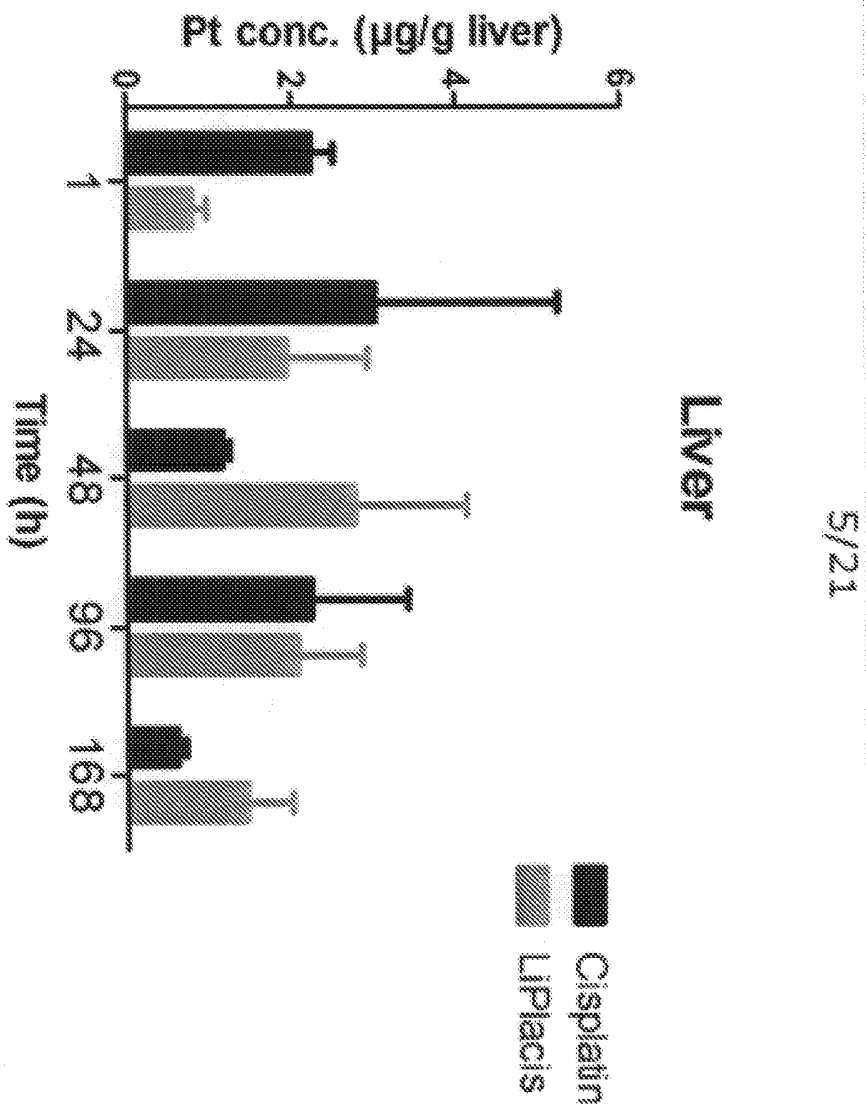


Figure 5

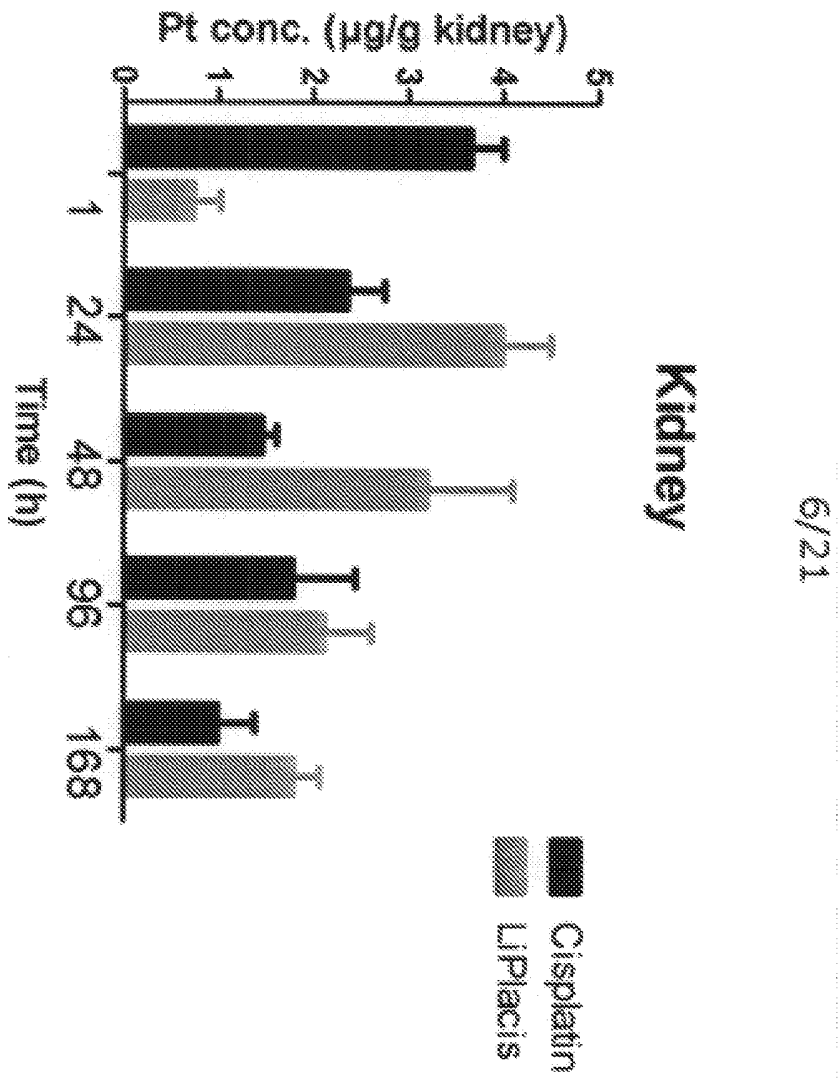


Figure 6

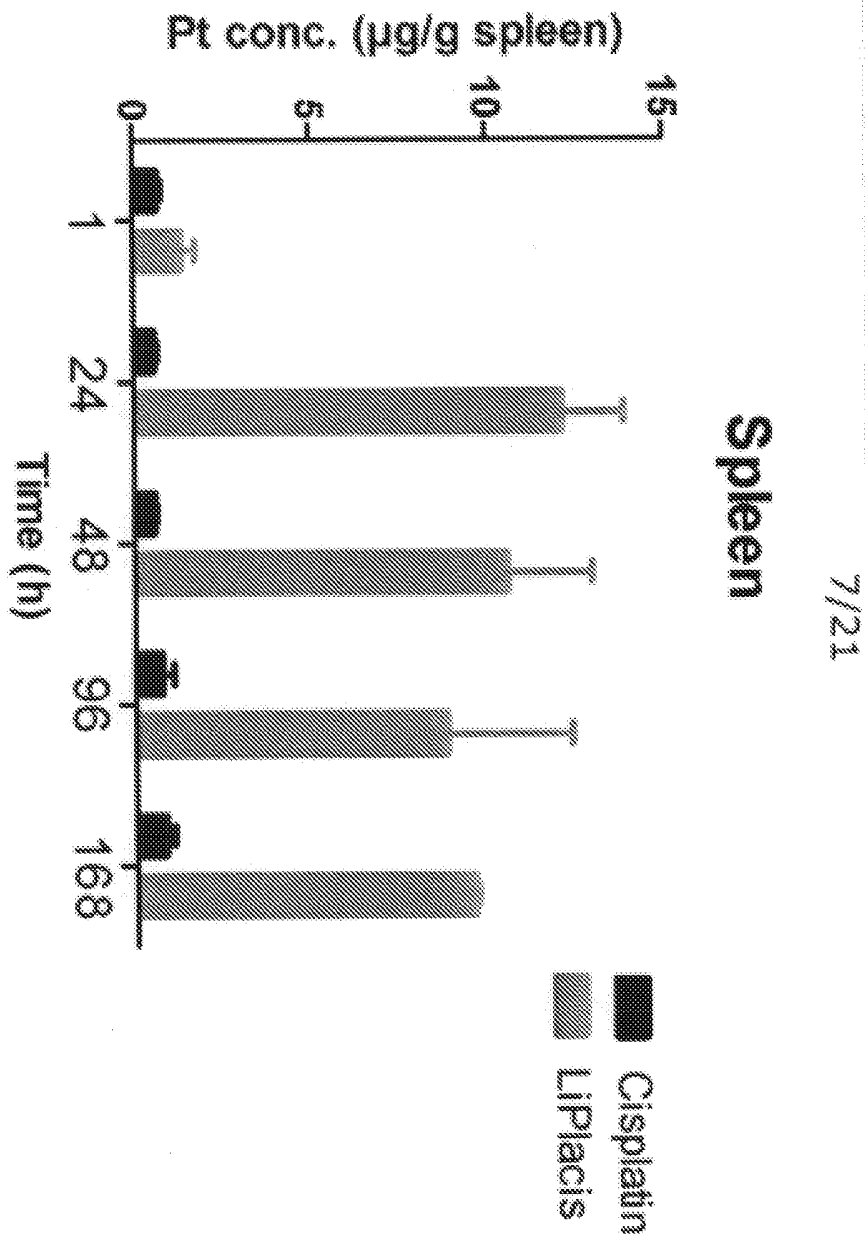


Figure 7

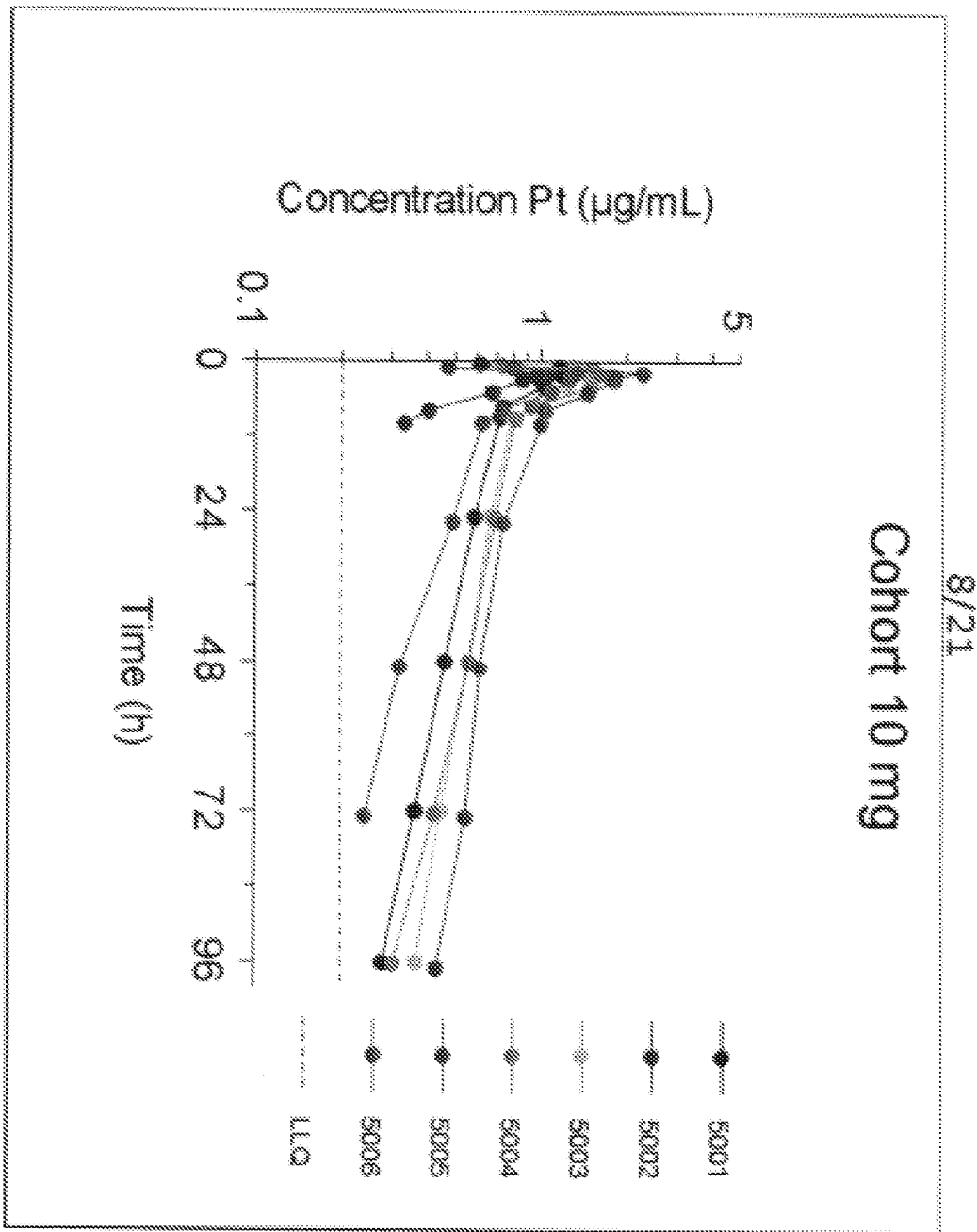


Figure 8

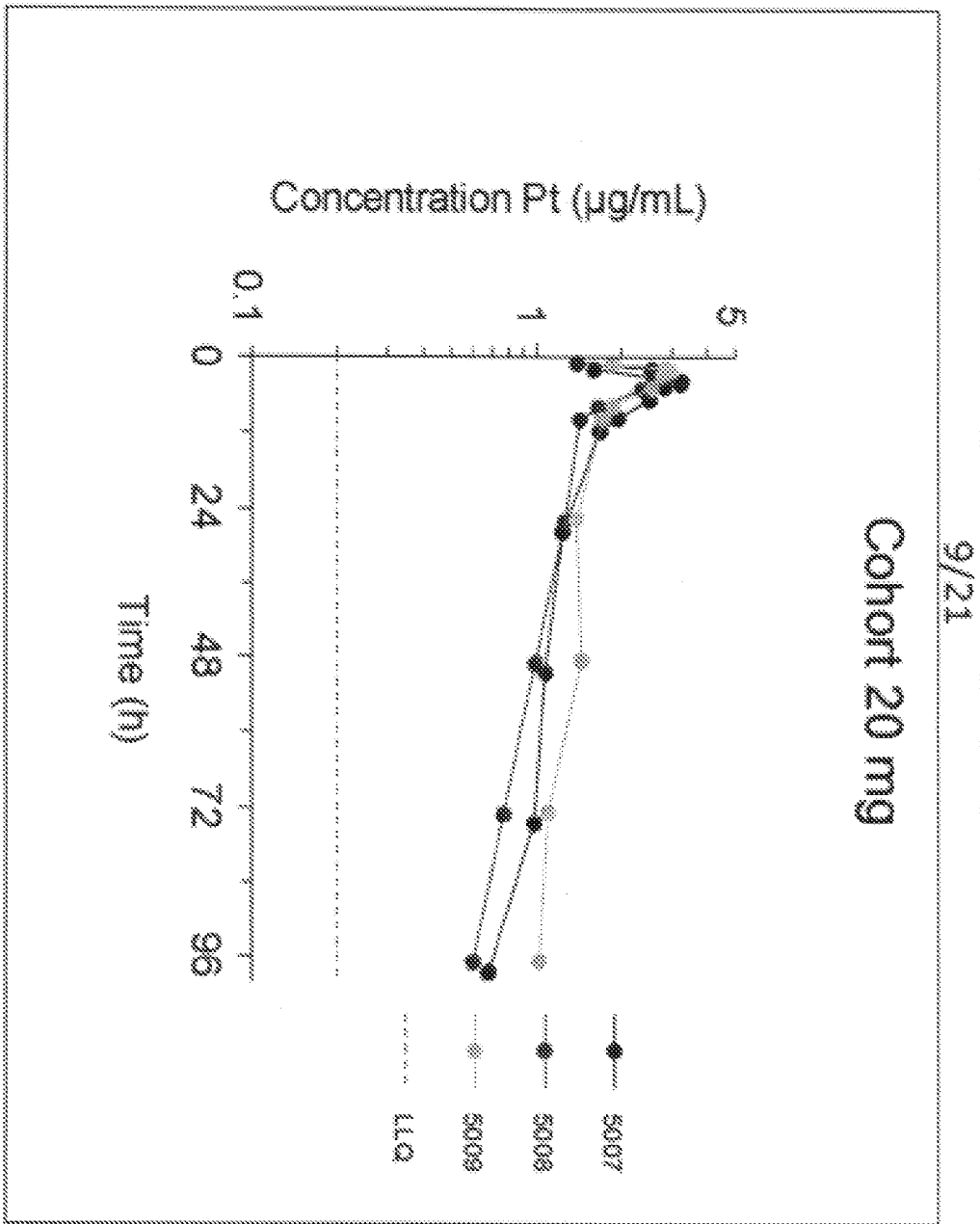


Figure 9

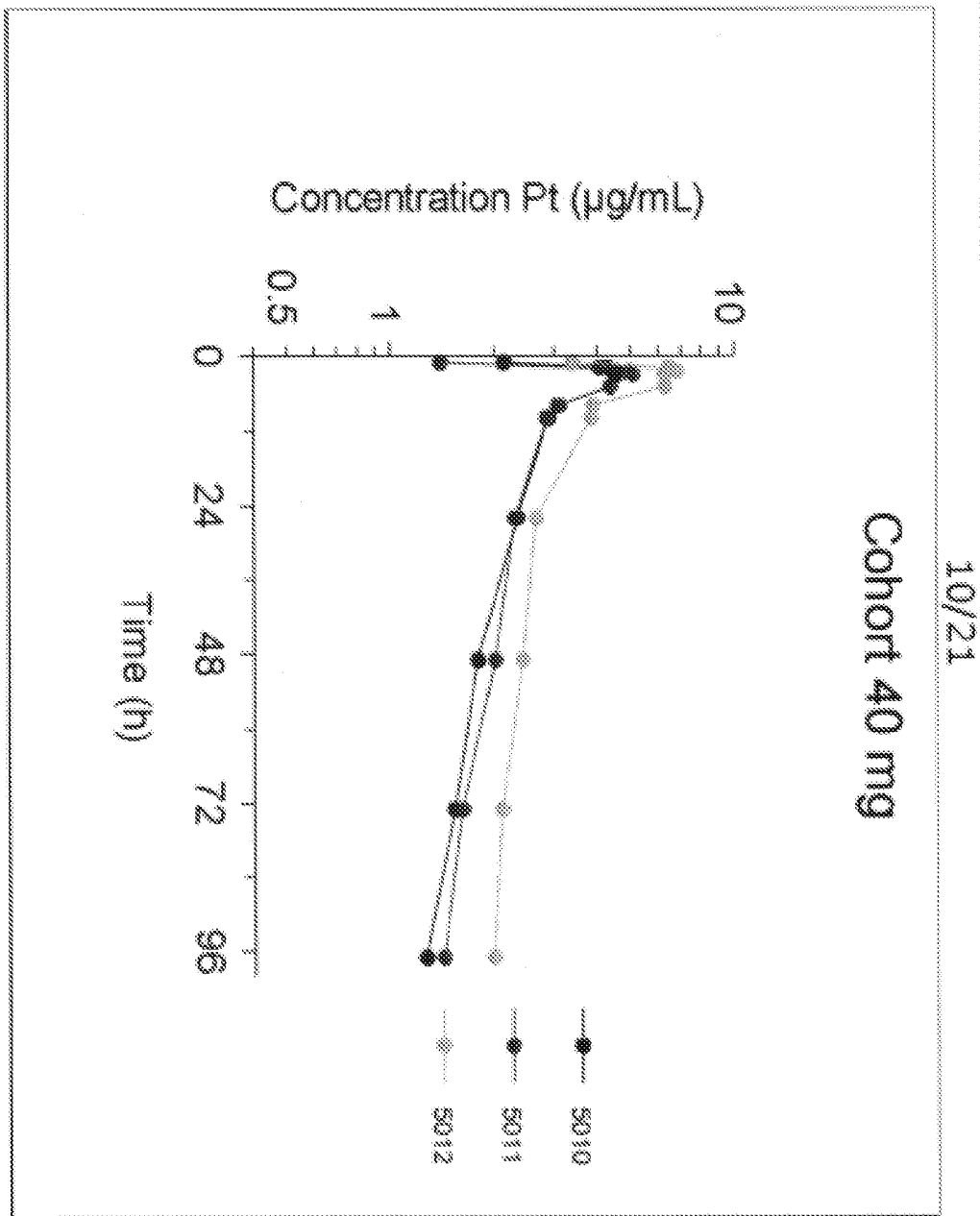


Figure 10

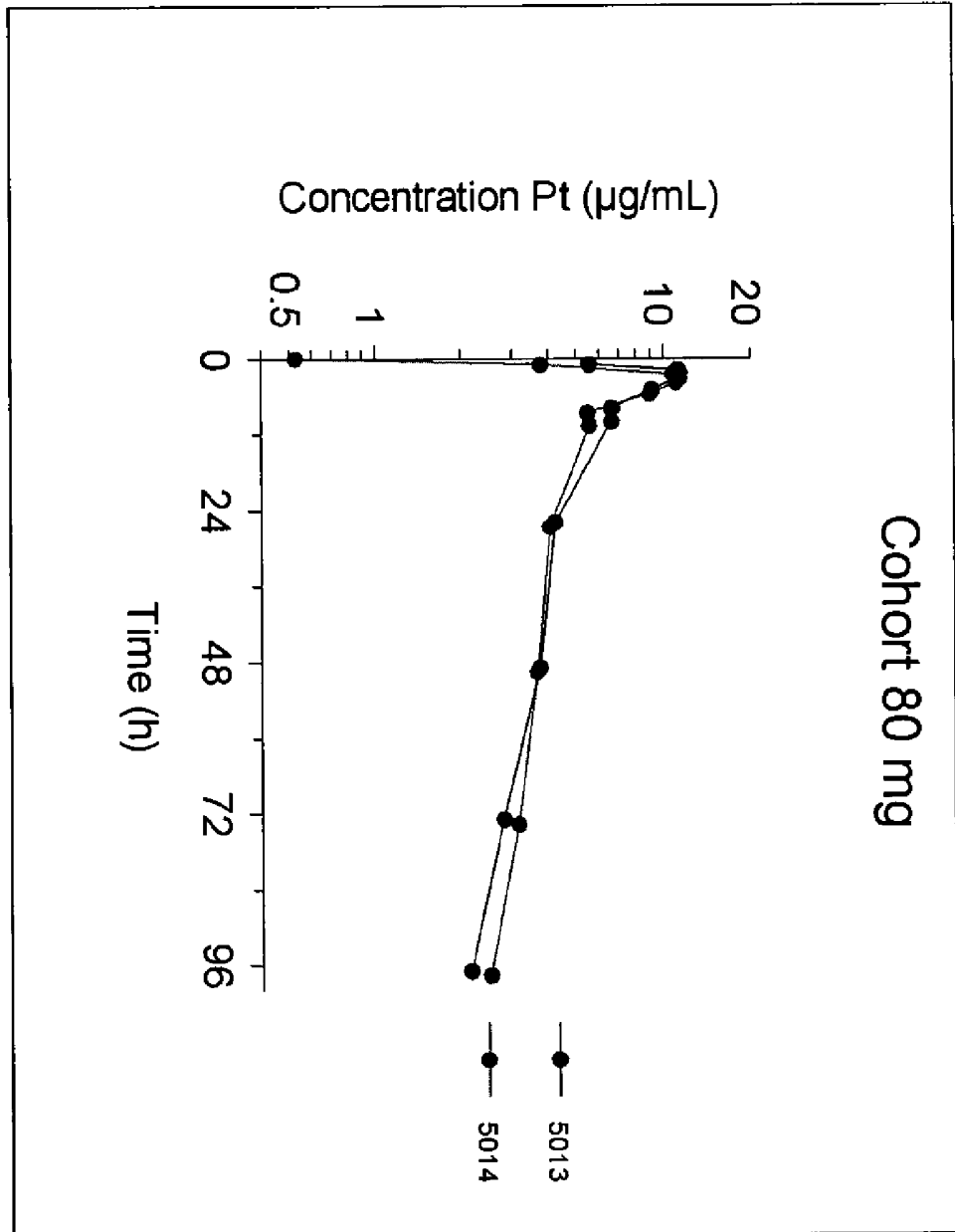
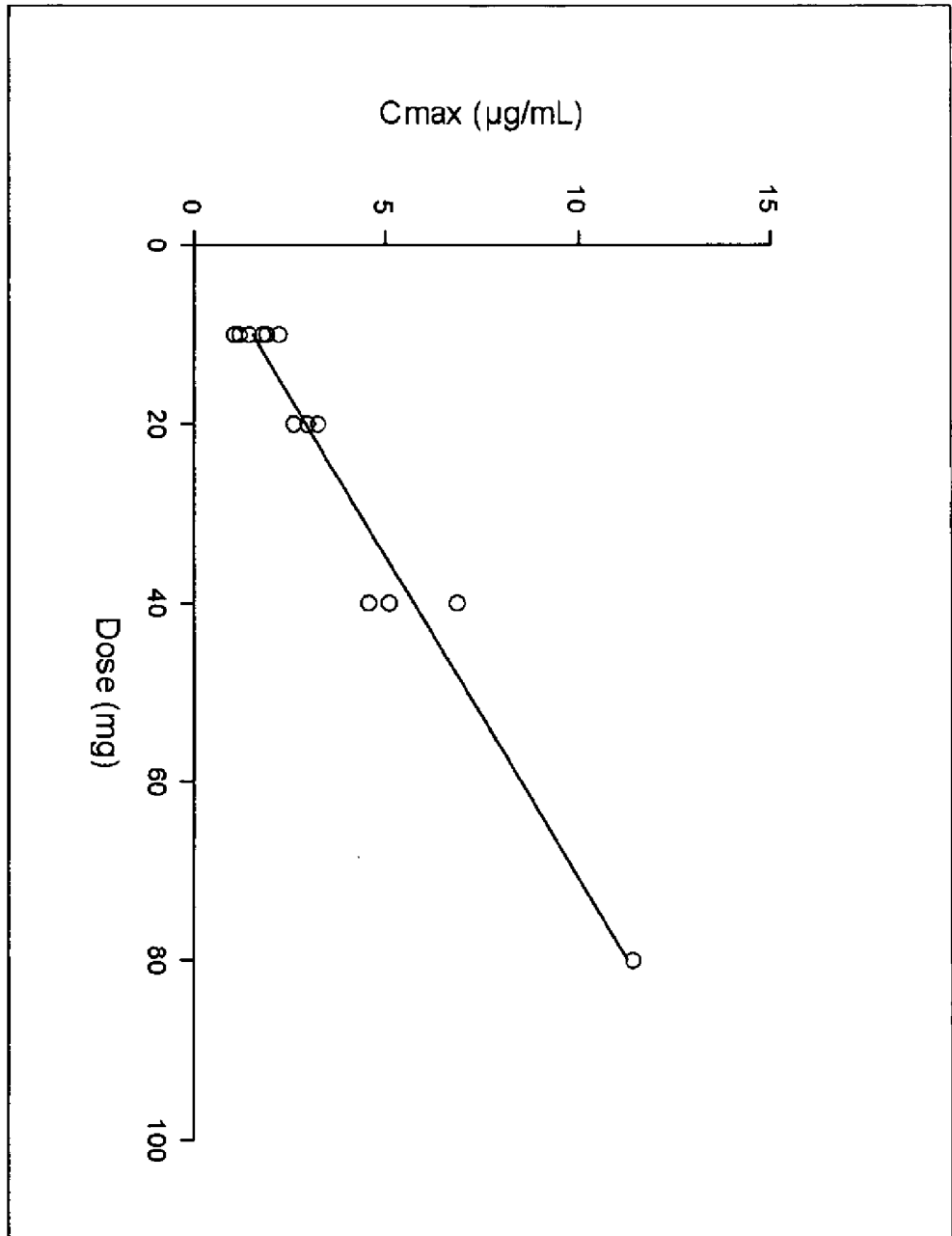
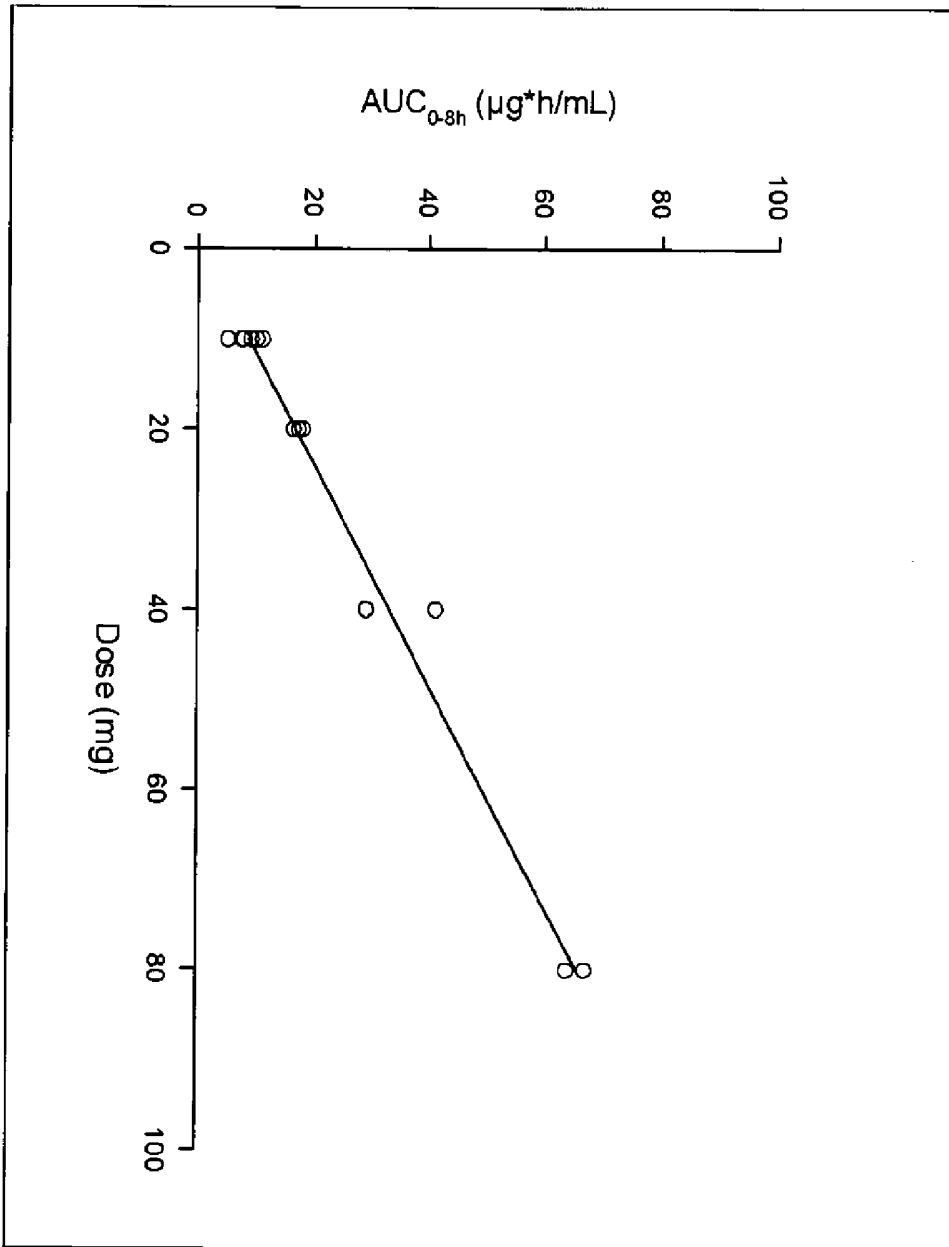


Figure 11



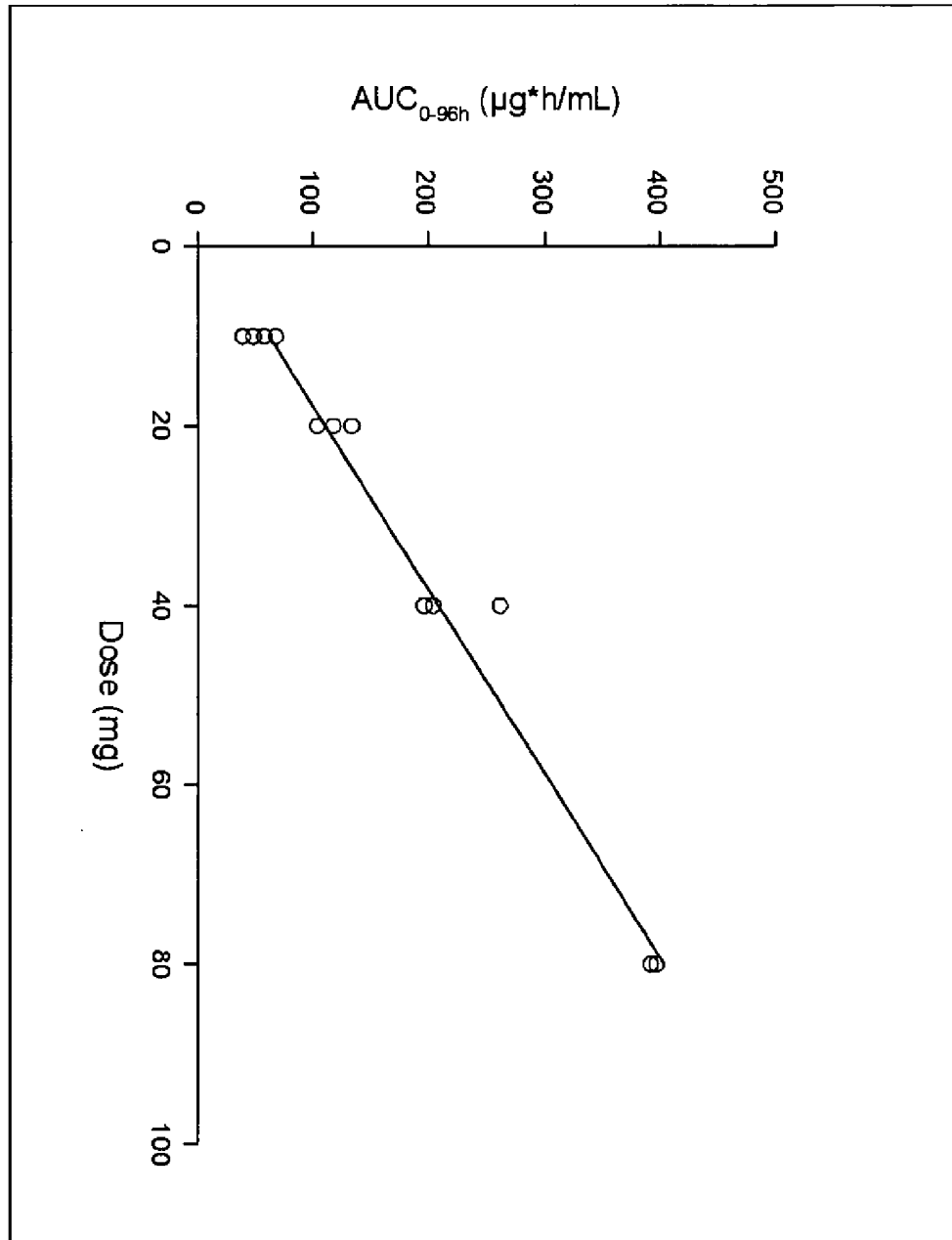
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Figure 12



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Figure 13



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Figure 14

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Subject No.	Gender	Age	Diagnosis	History of Cisplatin	Dose, mg/subject	1st Cycle	2nd Cycle	3rd Cycle	Comments
1	F	63	Breast Cancer	No	10	OK	OK	OK	PD
2	F	49	Melanoma	No	10	Allergic reaction, grade 2-3	Allergic Reaction, grade 3. DLT	Not done	Off study after 2 cycles
3	F	75	Adenoid Cystic Carcinoma	No	10	OK	OK	OK	PD after 15 cycles
4	M	51	Oesopharyngeal Cancer	No	10	OK	OK	OK	PD after 3 cycles
5	M	61	Prostate Cancer	No	10	Allergic reaction grade 2	OK	OK	PD after 6 cycles
6	F	44	Oropharyngeal cancer	No	10	OK	OK	Not done	Off study after 2 cycles due to PD
7	F	39	Parotid Cancer	?	20	OK	OK	OK	PD after 3 cycles
8	M	56	Urothelial-cell Cancer	?	20	OK	OK	OK	PD after 3 cycles
9	M	64	Parotid Cancer	?	20	OK	OK	OK	PD after 6 cycles
10	M	66	Melanoma	?	40	OK	OK	Not done	PD after 2 cycles
11	M	71	Prostate Cancer	?	40	OK	OK	Not done	Off-study after 2 cycles.
12	F	45	Breast Cancer	?	40	OK	Not done	Not done	Off study after first cycle. PD
13	M	62	Urothelial-cell Cancer	?	80	OK	OK	OK	
14	F	50	CUP	?	80	Allergic reaction grade 2	Allergic reaction grade 3	Not done	Off study after 2 cycles
15	M	53	Hypopharyngeal cancer	?	80	OK	OK	Pending	

Figure 15

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Pt. Nr.	Dose	Sex	Age	Tumor	Cyc le	Day	WBC	ANC	PLT	Hgb	Nau	Vom	Dia	Oral	Renal	Fever	Neuro	Fatigu e	Other	DLT	Respon s
3001	10 mg	F	63	breast	0		1	ASAT 2, ALAT 2, LDH 1		
					1		1	.	1	skin 1 (dry desquamation), ASAT 2, ALAT 2		
					2		1	AST 2, ALT 2		
					3		.	.	1	AST 1, ALT 1, LDH 1		PD
					off																
3002	10 mg	F	49	melanoma	0		pain 1		
					1		.	.	1	.	1	allergic reaction 3, rash 1, anorexia 1, AST 2, ALT 2, GGT 1	X	
					2														allergic reaction 3 (despite pre- medication), medication stop		
					off																
3003	10 mg	F	75	adenoidcystic carcinoma	0		GGT 1		
					1				
					2				
					3		AST 1, cholesterol 1		SD
					4		GGT 1, hypercholesterol 1		
					5		GGT 1, hypercholesterol 1		
					6		hypercholesterol 1		SD
					7		hypercholesterol 1		
					8		hypercholesterol 1		

Figure 16

