In vivo pharmacokinetics and biodistribution of gold nanoparticles

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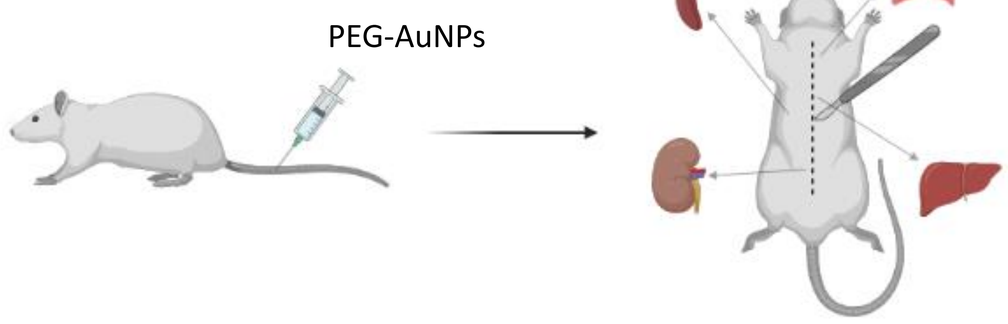
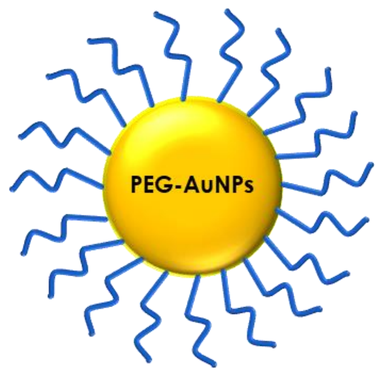
Introduction

The outstanding physicochemical properties, well-established synthetic procedures, and easy surface modifications make gold nanoparticles (AuNPs) an emerging platform for a wide range of pharmaceutical and biomedical applications. Despite the obvious advantages of gold nanoparticles for biomedical applications, controversial and incomplete toxicological data hamper their widespread use. Here, we present the results from an *in vivo* toxicity study using gold nanoparticles coated with polyethylene glycol (PEG-AuNPs).



Material

Nanomaterial
Core: gold sphere (10.5 ± 0.83 nm)
Coating: polyethylene glycol (PEG)
PEG-AuNPs



Animals
Wistar rats
Intravenous application
Dose 0.7 mg/kg (1 h, 4 h, 24 h, 7 days, and 28 days)
Collected: blood and organs/tissues (liver, lungs, spleen, kidneys)

Ananlysis
Quantification of PEG-AuNPs in the organism (AAS)
Pharmacokinetics of PEG-AuNPs
Histopathology

Results

Table 1. Body weight of control and PEG-AuNPs-injected rats

Group	Initial weight [g]	At 7 days [g]	P value	At 28 days [g]	P value
Control (PBS)	218.57 ± 11.00	247.50 ± 13.99	-	309.33 ± 15.50	-
PEG-AuNPs	229.28 ± 7.89	243.22 ± 19.19	0.644	288.33 ±18.06	0.122

Table 2. Gold amount in blood and organs per gram of tissue determined by GFAAS in rats at different time intervals after a single i.v. injection of PEG-AuNPs (0.7 mg/kg).

Organ	Gold concentration at particular time intervals [µg/g]				
	1 h	4 h	24 h	7 days	28 days
Blood	7.866 ± 1.316	2.792 ± 0.836	1.882 ± 0.385	0.052 ± 0.005	0.047 ± 0.013
Liver	1.546 ± 0.415	1.113 ± 0.293	1.380 ± 0.251	2.223 ± 0.260	2.153 ± 0.361
Lungs	2.954 ± 0.915	1.529 ± 0.230	1.099 ± 0.290	0.718 ± 0.153	0.904 ± 0.159
Kidneys	1.421 ± 0.178	0.819 ± 0.196	0.453 ± 0.115	0.209 ± 0.067	0.272 ± 0.023
Spleen	2.693 ±0.273	4.024 ± 1.337	10.594 ± 1.116	5.695 ± 1.037	4.410 ± 1.408

Table 3. Gold content in blood and organs determined by GFAAS in rats at different time intervals after a single i.v. injection of PEG-AuNPs (0.7 mg/kg).

Organ	The gold content in blood and organs at particular time intervals [µg]				
	1 h	4 h	24 h	7 days	28 days
Blood	126.172 ± 27.011	44.779 ± 17.162	30.184 ± 7.909	0.889 ± 0.073	0.955 ± 0.186
Liver	7.973 ± 0.824	5.737 ± 0.497	7.115 ± 1.293	11.460 ± 1.338	11.100 ± 1.145
Lungs	3.214 ± 0.995	1.663 ± 0.250	1.195 ± 0.316	0.782 ± 0.167	0.984 ± 0.173
Kidneys	1.521 ± 0.178	1.068 ± 0.255	0.591 ± 0.149	0.272 ± 0.087	0.354 ± 0.030
Spleen	0.986 ± 0.100	1.473 ± 0.328	3.877 ± 0.408	2.085 ± 0.379	1.616 ± 0.515

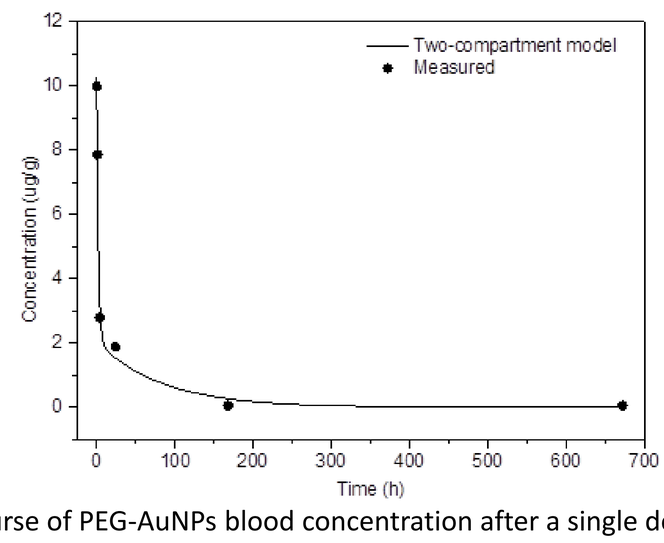


Figure 1. Time course of PEG-AuNPs blood concentration after a single dose i.v. administration (mean dose 204.8 µg). The solid line corresponds to least-squares fit by the two-compartment model.

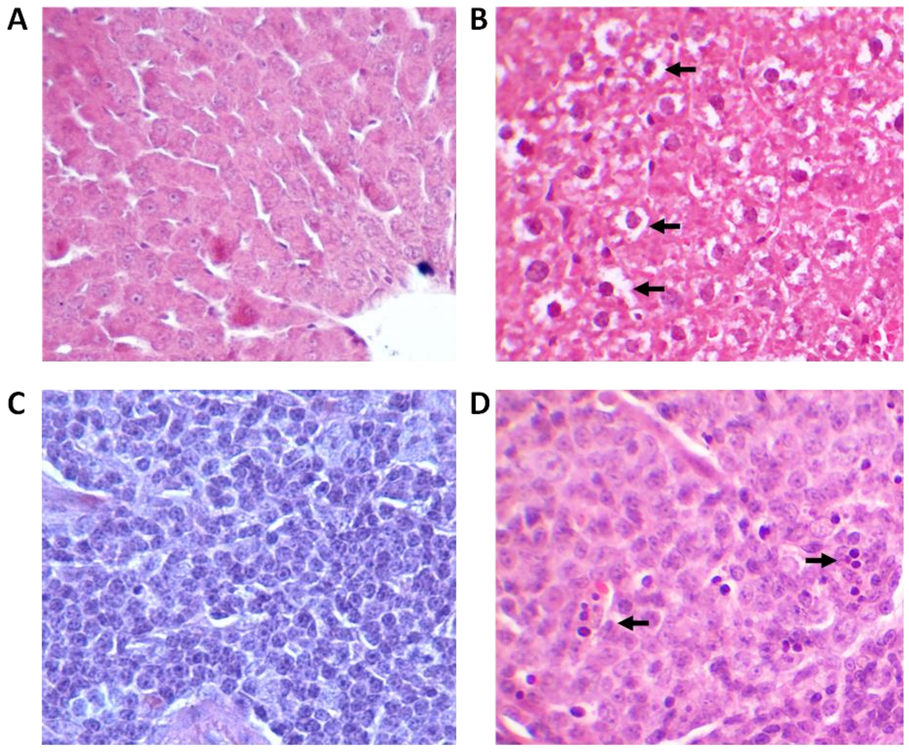


Figure 2. Histopathologic changes detected in the liver (A, B) and spleen (C, D) of PEG-AuNPs-exposed rats. Cytoplasmic vacuolation (arrows) observed in rat hepatocytes (A, B) at 7 days after single i.v. injection of PEG-AuNPs. Hematoxylin-eosin, magnification 20x.
Shrinking of cells (arrows) in the splenic white pulp (C, D) indicating apoptotic morphology observed in rat spleen 24 h after single i.v. injection of PEG-AuNPs. Hematoxylin-eosin, magnification 40x.

Conclusions

- ✓ PEG-AuNPs relatively slowly cleared from the blood and accumulated in all selected organs (mostly in the liver and spleen).
- ✓ a small amount of PEGAuNPs was detected even 28 days
- ✓ hepatotoxicity - histopathological changes determined in the liver
- ✓ the tissue accumulation of PEG-AuNPs might result in late toxic effects.

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