Submitted to small NANO MICRO

Supporting Information

Biocompatibility, Biodistribution and Drug Delivery Efficiency of Mesoporous Silica Nanoparticles for Cancer Therapy in Animals

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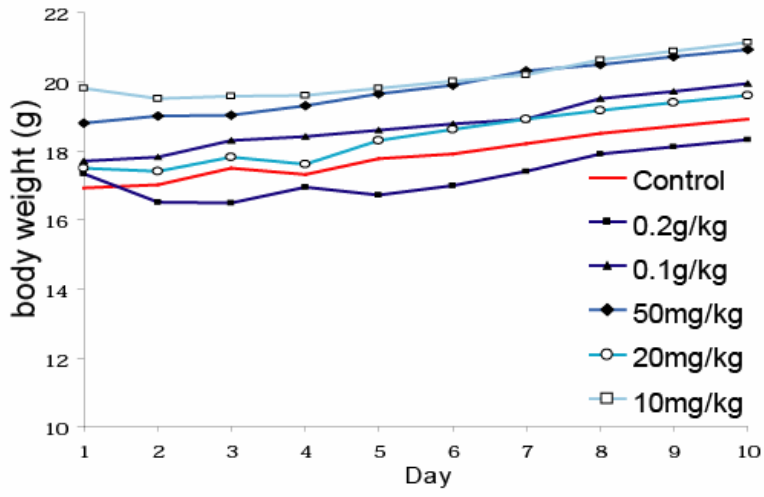
Figure 1

A



B

	control	0.2g/kg	0.1g/kg	50mg/kg	20mg/kg	10mg/kg	normal range
BUN (mg/dl)	20/21	21/21	20/20	18/18	21/21	22/22	8–33
CREAT (mg/dl)	0.1/0.1	0.2/0.2	0.1/0.1	0.2/0.2	0.2/0.2	0.2/0.2	0.2–0.9
GGT (U/L)	0.2/0.2	0.2/0.2	0.2/0.2	0.2/0.2	0.1/0.2	0.2/0.2	0-60
Albumin (g/dl)	3.6/3.7	3.9/3.9	3.8/3.8	3.2/3.2	3.4/3.4	3.5/3.5	2.5–5.4
ALT (U/L)	71/73	101/232*	27/277*	51/52	43/44	76/77	7–227
AST (U/L)	236/236	245/265	263/265	236/256	274/283	251/215	37–329
WBC (x1000)	12/12	12/12	13/13	12/12	12/12	12/12	6–15
monos (%)	3/3	3/3	2.5/2.5	2.6/2.6	2.3/2.3	2.4/2.4	1–4
lymphs (%)	72/71	71/71	73/73	75/75	73/73	71/71	55–95

Figure 1. Determination of the maximum tolerated dosage of FMSNs. Mice were injected (i.v.) with various doses, ranging from 4 mg/mouse (approximate 200 mg/kg) to 0.25 mg/mouse (approximate 10 mg/kg), once per day for 10 days. **A.** The mouse body weights are shown. **B.** Serological and hematological results of mice are shown. * indicated abnormality.

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Figure 2

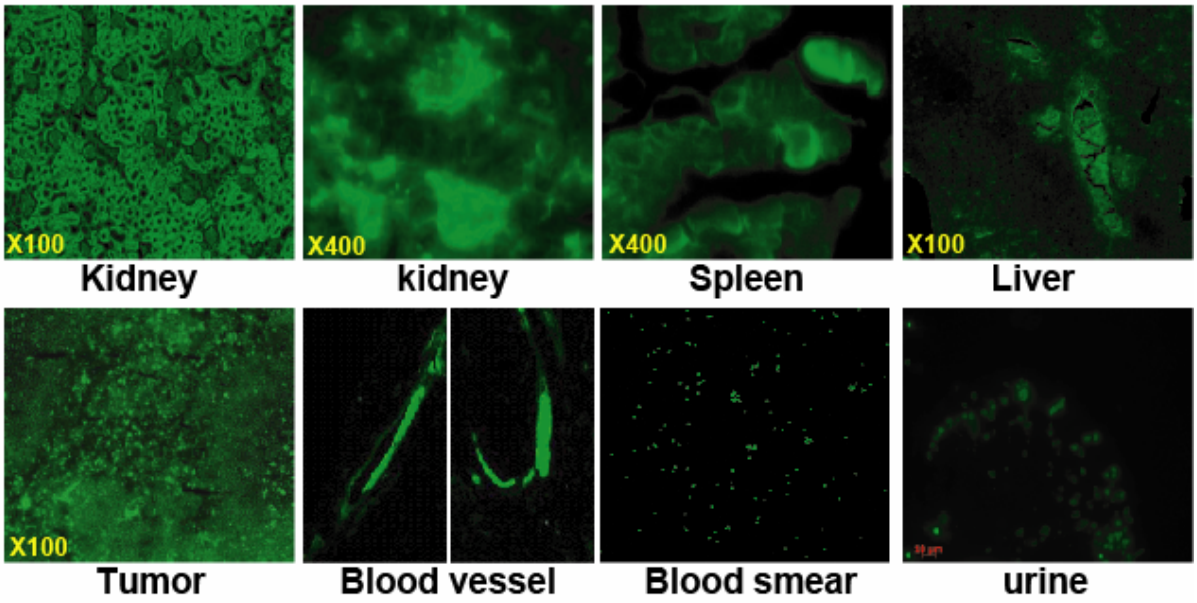

Figure 2. Representative fluorescent images of mouse's organs and tumors. The fluorescent nanoparticles were highly condensed in the glomerulus of kidney. In spleen, particles were observed mostly in the red pulp. In liver, they were concentrated in portal vein. In contrast, the particles were evenly observed in the tumors, inside of cells as well as interstitial space. On the other hand, strong fluorescent signal was observed in blood vessels even after 72h. The detection of green fluorescence in smear of urine collected from bladder confirmed the observed the renal excretion route.

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Table 2

Table 2. Histopathological reports of mice treated with MSNs for 14 days.

	control	Treated mice				
i.v.	**0**	**1mg/mouse**	**0.5mg/mouse**	**0.25mg/mouse**	**0.1mg/mouse**	**0.05mg/mouse**
Gross Diagnosis	No gross abnormalities	No gross abnormalities	no gross abnormalities	No gross abnormalities	1.No gross abnormalities. 2.Hepatomegaly based on percentage of body weight	1.No gross abnormalities. 2.Hepatomegaly based on percentage of body weight
Histological diagnosis	Hepatic Bile Duct Hyperplasia, subacute, moderate.	Hepatic Bile Duct Hyperplasia, subacute, mild	1. pulmonary hemorrhage, acute, multifocal, mild to moderate. 2. Hepatic Bile Duct Hyperplasia, subacute, mild to moderate	1. Pulmonary Hemorrhage, acute, multifocal, mild 2. Hepatic Bile Duct Hyperplasia, subacute, mild to moderate	Pulmonary Venous Thrombus, acute, focal	No histologic lesions
Comment by Pathologist	no histologic lesions within any of the other tissues examined	no histologic lesions within any of the other tissues examined	no histologic lesions within any of the other tissues examined	no histologic lesions within any of the other tissues examined	The thrombus in this pulmonary vessel was not associated with any pathology and was not organized or covered by endothelium. No other thrombi were noted within any of the other tissues examined.	no histologic lesions within any of the other tissues examined

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Table 3. Representive histopathological, serological and hematological results of mice.

Necropsy:	Control 1		CPT treated		MSNs-treated		FMSNs+CPT treated		F-FMSNs+CPT treated	
	1	2	1	2	1	2	1	2	1	2
% of Body Weight										
Body Weight (g)	20.36	21.75	18.77	18.63	20.37	20.37	20.02	18.55	21.97	21.42
Liver	7.96%	6.85%	7.19%	7.09%	7.27%	7.27%	7.79%	7.01%	7.42%	6.63%
Spleen	1.13%	0.64%	0.59%	0.64%	0.54%	0.54%	0.70%	0.54%	0.68%	0.75%
Pancreas	0.79%	1.06%	0.69%	0.86%	0.59%	0.59%	1.10%	0.27%	1.09%	1.26%
R Kidney	0.93%	0.87%	0.80%	0.97%	0.93%	0.93%	0.85%	0.54%	0.91%	0.84%
L Kidney	0.93%	0.87%	0.91%	0.86%	0.93%	0.93%	0.90%	0.97%	0.73%	0.84%
R adrenal	present	present	present	present	present	present	present	present	present	present
L adrenal	present	present	present	present	present	present	present	present	present	present
Brain	2.11%	1.98%	2.13%	2.36%	2.16%	2.16%	2.00%	2.10%	2.09%	2.01%
Heart	0.74%	0.69%	0.85%	0.86%	0.59%	0.59%	0.70%	0.81%	0.68%	0.75%
Necropsy Findings:	mildly enlarged spleen.	mildly enlarged sub-mandibular lymphnodes	mildly enlarged right submandibular and left ax lymph nodes	The spleen has a prominent white pulp.	The spleen has a prominent white pulp.			The right kidney is small and the left kidney is mildly enlarged.	mildly enlarged spleen.	mildly enlarged spleen.
Ancillary Test:	mild hypoalbuminemia	mild erytrhocytosis, moderately elevated hematocrit, moderately decreased levels of creatinine kinase	mild neutrophilia, moderate elevation of hematocrit, RBC and hemoglobin levels and mildly elevated levels of creatinine kinase.	1. Erythrocytosis, hemoglobinemia and elevated hematocrite, mild 2. Elevated liver enzymes (ALT, AST), moderate to severe 3. Hypoalbuminemia and hypoproteinemia, moderate to severe 4. Elevated Creatinine Kinase, mild 5. Decrease levels of calcium and phosphorus, mild to moderate	1. Elevated hematocrite, mild 2. Elevated liver enzymes (ALT, AST), mild	1. Elevated hematocrite, mild 2. Elevated liver enzymes (ALT, AST), mild	1. Elevated hematocrite, mild 2. Elevated liver enzymes (AST), severe	1. Elevated liver enzymes (AST, ALT), mild to moderate.	1. Elevated liver enzymes (AST, ALT), severe. 2. Increased hematocrite level, mild 3. Neutrophilia, mild.	1. Mildly elevated hematocrite levels
Gross Diagnosis:	1. Splenomegaly, subacute, mild, 2. Hepatomegaly, subacute, mild to moderate 3. Bilateral renomegaly, subacute, mild 4. Cradiomegaly, subacute, mild	1. Hepatomegaly, subacute, mild to moderate 2. Splenomegaly, subacute, mild, 3. Bilateral renomegaly, subacute, mild to moderate 4. Cardiomegaly, subacute, mild	1.Hepatomegaly, subacute, moderate 2.Bilateral renomegaly, subacute, moderate 3.Cardiomegaly, subacute, moderate	1.Hepatomegaly, sub acute, moderate 2.Bilateral renomegaly, sub acute, moderate 3.Cardiomegaly, sub acute, moderate	1. Hepatomegaly, sub acute, moderate 2. Bilateral Renomegaly, mild	1.Hepatomegaly, subacute, moderate 2.Bilateral Renomegaly, mild	1.Hepatomegaly, sub acute, moderate. 2.Splenomegaly, sub acute, mild to moderate. 3.Bilateral renomegaly, sub-acute, moderate. 4.Cardiomegaly, sub-acute, mild to moderate.	1.Left renomegaly, chronic, mild to moderate. 2.Renal atrophy, right kidney, chronic, mild 3.Hepatomegaly, sub acute, mild. 4.Cardiomegaly, sub-acute, mild to moderate.	1.Hepatomegaly, sub acute, mild. 2.Splenomegaly, sub-acute, mild. 3.Bilateral renomegaly, sub-acute, mild to moderate. 4.Cardiomegaly, sub-acute, mild.	1.Hepatomegaly, sub acute, mild. 2.Splenomegaly, sub-acute, mild. 3.Bilateral renomegaly, sub-acute, mild to moderate. 4.Cardiomegaly, sub-acute, mild.
Histological diagnosis	No abnormal finding	1. Adrenal Cortical Fibosis, chronic, unilateral, mild 2. Lymph Node Cyst 3. Lymphoid Hyperplasia, mesenteric, moderate	1. Lymphoid Hyperplasia, extra nodal, mild 2. Mesenteric Lymphoid Hyperplasia, chronic, plasmacytic with Mott cells, moderate to severe 3. Adrenal Capsular Fibrosis, chronic, moderate to severe	1. Lymphoid Hyperplasia, nodal, plasmacytic, moderate 2. Adrenal Capsular Fibrosis, chronic, bilateral,mild to moderate	1. Gastritis, chronic, multifocal, mild to moderate 2. Adrenal Capsular Fibrosis, bilateral, mild	1. Gastritis, chronic, multifocal, mild to moderate 2. Adrenal Capsular Fibrosis, bilateral,	1. Adrenal Capsular Fibrosis, chronic, moderate 2. Renal Interstitial Fibrosis, 3. Splenic Lymphoid Depletion,	1. Gastric Epithelial Hyperplasia and Orthokeratosis, moderate, chronic, 2. Renal Interstitial Fibrosis, chronic, 3. Adrenal Capsular Fibrosis		1. Adrenal Capsular Fibrosis, chronic, mild to moderate 2. Myoepithelioma - submandibular salivary gland
Comments By Pathologist		Elevated levels of Hematocrite, RBC and hemoglobin are typically associated with dehydration		The increased levels of liver enzymes, moderate to severe hypoalbuminemia and hypoproteinemia, and hepatomegaly based on percentage of body weight are indicative of hepatitis.	The increased levels of liver enzymes and hepatomegaly based on percentage of body weight can be indicative of hepatitis, however these changes are mild and therefore may be nonsignificant.		The severe increased levels of liver enzyme and hepatomegaly based on percentage of body weight can be indicative of hepatitis	The severe increased levels of liver enzymes and hepatomegaly based on percentage of body weight can be indicative of hepatitis	The increased levels of liver enzymes, moderate to severe hypoalbuminemia and hypoproteinemia, and hepatomegaly based on percentage of body weight are indicative of hepatitis.	