Characterization of Pentagalloyl glucose (PGG) loaded BSA nanoparticles as targeted therapy for abdominal aortic aneurysm (AAA) regression

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Statement of Purpose: Degeneration of elastin plays a crucial role in the pathology and progression of aortic aneurysms, a disease characterized by the loss of structural integrity of the arterial wall. Pentagalloylglucose (PGG), a derivative of tannic acid, has been shown to hinder the development of AAA in a clinically relevant animal model [1]. Stabilization of aortic elastin in aneurysmal arterial segments offers great potential for the development of effective therapies for stabilization of AAAs. We propose an approach to deliver PGG to the site of AAA by using targeted nanoparticles as a treatment option to prevent further disease progression and reverse the elastin damage [2]. Toward this aim, we have optimized BSA nanoparticles loaded with PGG.

Methods Bovine serum albumin nanoparticles were prepared by coacervation following two different processes named method A and B.

Method A: Nanoparticles were obtained by dissolving 250 mg Bovine serum albumin (BSA; Seracare, MA, USA) in 5 mL DI water. 125 mg Pentagalloyl glucose (PGG) was dissolved in 400 µL DMSO and added to BSA solution and stirred for 1 h. The aq. solution was added dropwise to 30 mL of ethanol under continuous sonication (Omni Ruptor 400 Ultrasonic Homogenizer) (Omni International Inc, Kennesaw, GA) and sonicated for 30 min. For crosslinking, glutaraldehyde (12 µg/mg protein) (EM grade 70%, EMS, PA, USA) was added either during the first hour of stirring or during 30 minutes of sonication.

Method B: Nanoparticles were obtained as mentioned above. For crosslinking, glutaraldehyde was added during sonication with different concentrations of 0.36, 0.7, 1 and 100 µg glutaraldehyde per mg BSA. NPs were characterized for their size, surface charge, drug loading, release, cytotoxicity, and macrophage uptake.

Results: Nanoparticle yield and % loading are shown in Table 1. Batch B4 did not produced nanoparticles and resulted in a paste. Data clearly show NP yield, % loading and PGG release profile is highly dependent on timing and concentration of glutaraldehyde Adding the cross linker before sonication increases both the loading and yield, while increasing the amount of the cross linker added during the sonication step increases just the yield and not the loading. Increasing the amount of glutaraldehyde, when adding the cross-linker during sonication results in higher percentage yield and loading, for small amount of glutaraldehyde.

	A1	A2	B1	B2	B3	B4
Glut	12 ug/mg BSA	12 ug/mg BSA	0.36 ug/mg BSA	0.72 ug/mg BSA	1 ug/mg BSA	100 ug/mg BSA
Glut added Before sonication	*					
Glut added While sonication		*	*	*	*	
Sonication time	30 min	30 min	30 min	30 min	30 min	
Loading %	37.92±0.8	11.77±3.2	24.9±1.11	26.02±3.6	42.45±1.71	
Yield%	61.0±3.2	51.1±2.2	15.73±4.7	18.49±0.4	20.44±1.3	

Table 1. Nanoparticle characterization

Figure 1 shows the release profile for PGG from different batches of nanoparticles. The drug released within 5 days with burst release in first few hoursfrom all batches of NPs except for A1. A1 batch showed prolonged release that lasted for 60 days. It is evident that adding the glutaraldehyde before sonication resulted in a slower release as compared to the methods in which glutaraldehyde was added during sonication.

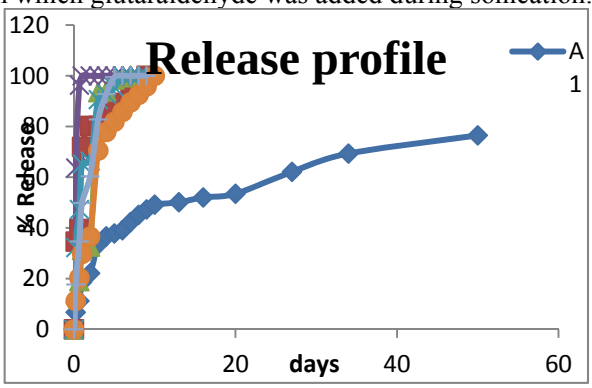

Figure 1: Release profile for PGG from NPs.

Conclusions:

We can control PGG loading and release from BSA nanoparticles by varying time of addition and concentration of glutaraldehyde. These NPs will be used as promising agents for drug delivery in AAA conditions.

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References:

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