TREATMENT OF GLIOBLASTOMA USING IRON OXIDE NANOPARTICLES

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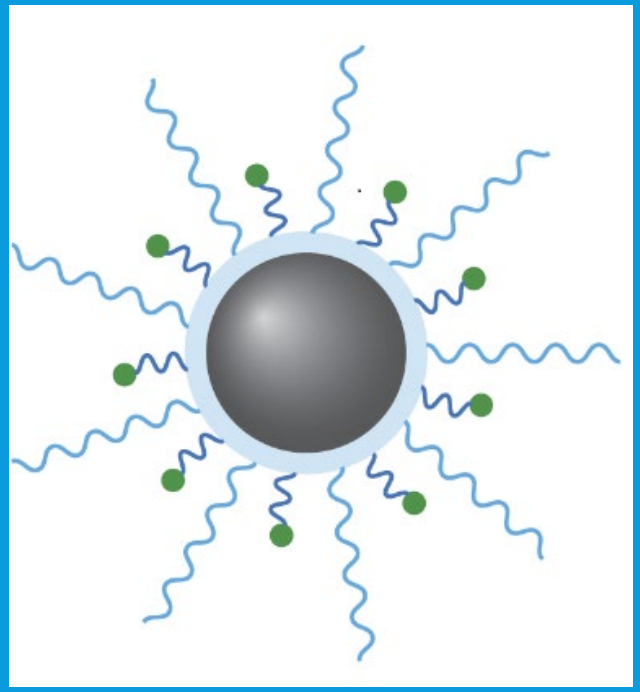
BACKGROUND

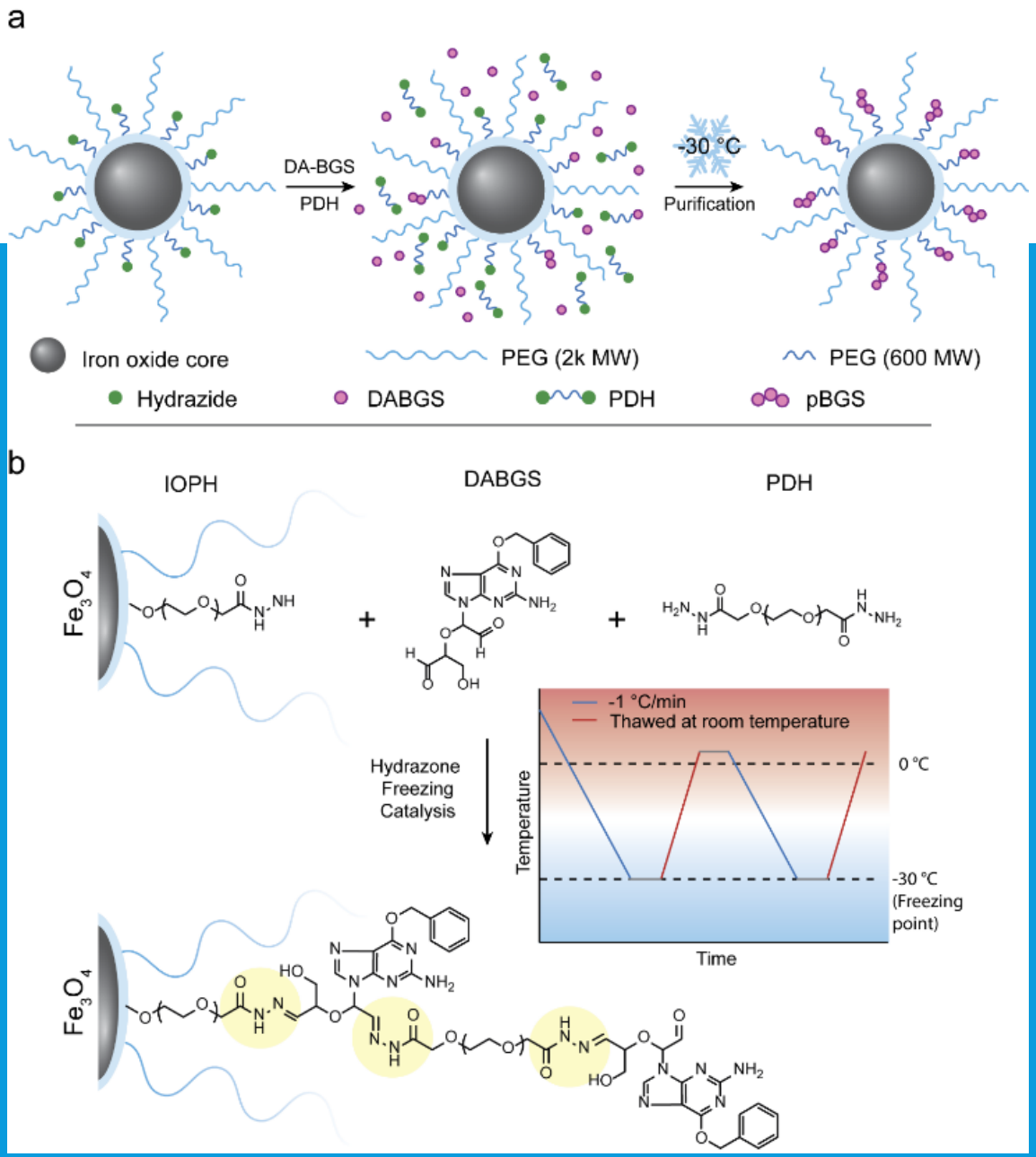
- Glioblastoma (GBM) tumors affect 14,000 individuals in the U.S. each year
- Current treatments include a combination of radiation therapy, chemotherapy, and surgery
- GBMs present many challenges to the current therapeutic approaches that have become the standard of care
  - Lack of targeting causes offsite accumulation of the drug
  - Many patients are resistant to the chemotherapeutic drug temozolomide (TMZ) due to the DNA repair agent O^6-methylguanine DNA methyltransferase (MGMT)
- Iron-oxide nanoparticles formulated with MGMT inhibitor O^6-benzylguanine (BG) have the potential to increase the efficacy of TMZ and provide a less invasive route to better clinical outcomes

APPROACH

- Superparamagnetic iron-oxide nanoparticles (SPIONs)
- Iron-oxide core: allows particles to be detected through MRI imaging; iron-oxide is also biodegradable and biocompatible which makes it ideal for *in vivo* applications
- Polyethylene glycol: polymer coating makes particles biocompatible and water soluble
- Functional groups attached to polymer
  - O^6-benzylguanosine (BGS) is a modified version of BG which makes the nanoparticles functional in inhibiting the activity of MGMT

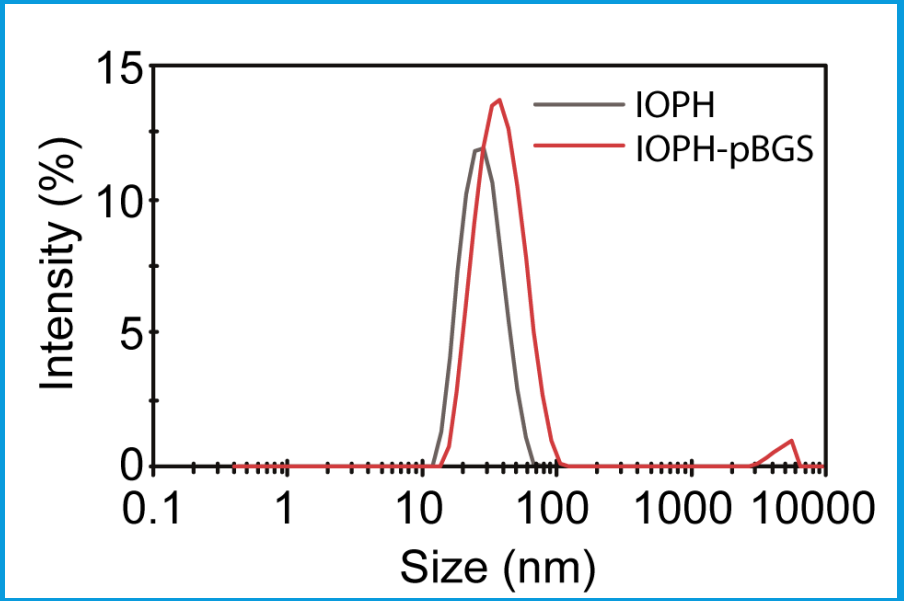


SCHEMATIC


a
DA-BGS
PDH
-30 °C
Purification
Iron oxide core
PEG (2k MW)
PEG (600 MW)
Hydrazide
DABGS
PDH
pBGS
b
IOPH
DABGS
PDH
Hydrazone
Freezing
Catalysis
-1 °C/min
Thawed at room temperature
0 °C
-30 °C
(Freezing
point)
Temperature
Time

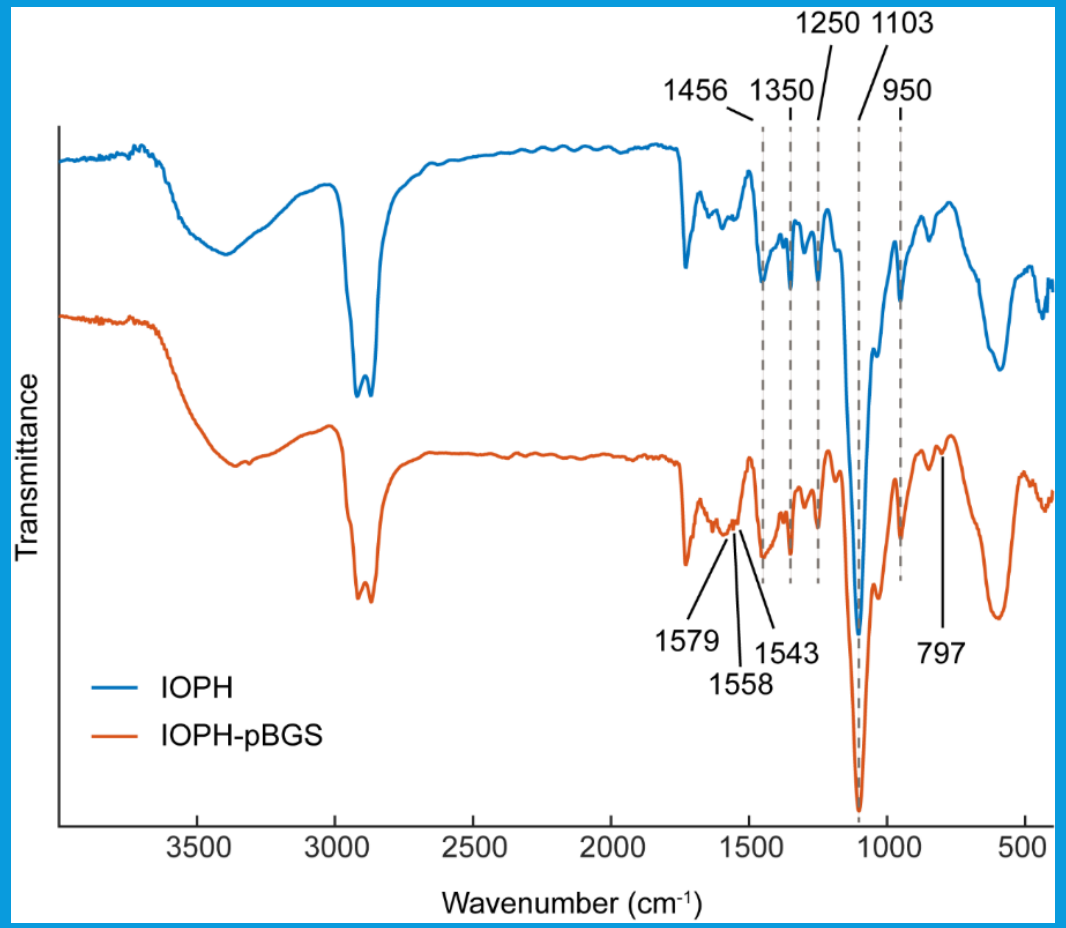
CHARACTERIZATION

- Before synthesized particles could be used for *in vitro* and *in vivo* experiments they were evaluated on size, presence of functional groups, and drug loading
- Size
  - DLS measurements were taken to measure the average size of the synthesized particles and to determine the stability of the particles
  - The IOPH-pBGS particles were found to have an average size of 36.5 ± 1.8 nm in HEPES buffer, pH 7.4



CHARACTERIZATION

- Presence of functional groups
  - Fourier Transform Infrared Spectroscopy (FTIR) spectra were used to verify the presence of conjugated molecules
  - Bands at 1579, 1558, 1543, and 797 cm-1 on the FTIR spectra indicate the presence of BGS on the surface of the particles
- Drug loading
  - BGS loading was measured using UV-vis spectroscopy
  - The percent drug loading per nanoparticle was determined to be 38.3 ± 2.9 wt%



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DRUG QUANTITATION

- Standard Addition Method
  - Polymerized BGS degraded from surface of nanoparticle and collected through a spin filter
  - Absorbance on sample from nanoparticle was compared to samples of known drug concentrations.