A Phosphorylcholine Polymer Platform for Cancer Drug Delivery

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A Phosphorylcholine Polymer Platform for Cancer Drug Delivery

Todd Emrick & Sallie Schneider
UMass Amherst Polymer Science and Engineering
and the Pioneer Valley Life Sciences Institute
PolyMPC: current applications and future potential

PolyMPC is extremely hydrophilic and biocompatible: Ishihara, Nakabayashi, Iwasaki, Armes, Lewis,..
Why Polymers? Polymers Enhance Drug Delivery
Prolonged Circulation; Enhanced Permeation and Retention

Normal vessels have tight junctions between cells – allow minimal extravasation into healthy tissue

Tumor vessels are disorganized and leaky

Polymer-drug conjugates are large and are taken up into tumor tissue

Passive targeting

Normal vessels

Tumor vessels

pH ~ 7.4

pH ~ 6.0 - 6.8

Polymer/drug flow through capillary

~ < 400 nm
PolyMPC-CPT: the first polyMPC pro-drug

Drug loading: 18 wt %, CPT equivalent solubility: 36.7 mg/mL

Drug loading: 3.7 wt %, CPT equivalent solubility: 6.7 mg/mL
PolyMPC-Doxorubicin pro-drugs

**Labile bond**

**Bioconjugate Chemistry 2012**

DOX release from polyMPC-DOX conjugates at pH 5.0 and 7.4

Half-life of polyMPC-Dox samples range from 8-28 hours, depending on molecular weight and drug loading

PolyMPC-Dox soluble in water and injectable saline at very high DOX loading
In vitro and in vivo evaluation

**Cell uptake** MCF7 24 h

(a) Pro-drug
(b) Pro-drug
(c) DOX

**Maximum tolerated dose (MTD) of polyMPC-Dox**

- Nuclear uptake seen for polyMPC-Dox
- MTD values of 50 mg/kg or greater
- About 10 times that of Dox alone
- About twice that of Doxil

*Bioconjugate Chemistry 2012*
In vivo experiments in mice: 4T1 breast cancer model

Highly invasive and spontaneously metastatic tumor line
Large tumor starting volume; 1 injection

Survival
Doxil: 40% at 7 days, 0% at 14 days
polyMPC-Dox: 100% at 7 days
50% at 14 days

Survival
Day 15 with Dox: 10% survival
Day 15 with polyMPC-Dox: 90% survival