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

Current

Contact lenses
Proclear (Copper Vision)

Stent devices
Endeavor (Medtronic)
Trimaxx and Dexamet (Abbott)
BiodivYsio (Biocompatibles)

PolyMPC is extremely hydrophilic and biocompatible: Ishihara, Nakabayashi, Iwasaki, Armes, Lewis,

Future

Longer lasting protein therapeutics
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.

Polymer/drug flow through capillary.

pH ~ 7.4

pH ~ 6.0 - 6.8

~ < 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

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

**Doxil**
- 40% at 7 days, 0% at 14 days

**polyMPC-Dox**
- 100% at 7 days
- 50% at 14 days

**Balb/c-4T1 efficacy: Tumor Volume**

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