AqueaTether™

SUPER HYDROPHILIC MONO-DISPERSED BIOCOMPATIBLE HIGH-LOADING

AqueaTether™ therapeutics constructs novel proprietary biomaterials and innovative chemical architectures from a class of natural and edible sugar alcohol compounds, called AqueaTether™ (AqT™) molecules. AqT™ molecules are designed to load, connect, or modify both small molecule hydrophobic drugs or larger molecule biologics to create a new hybrid drug entity with an improved therapeutic profile.

Patent protection for the composition matter of AqT™ molecules and their conjugates: Issued patents **US**8907079 B2, **US**14/156,224, **US**15/281,023, **CN** 201280034231.3, **AU** 2012284055, **JP** 2014-521744. Pending in EU, Brazil, and Canada.

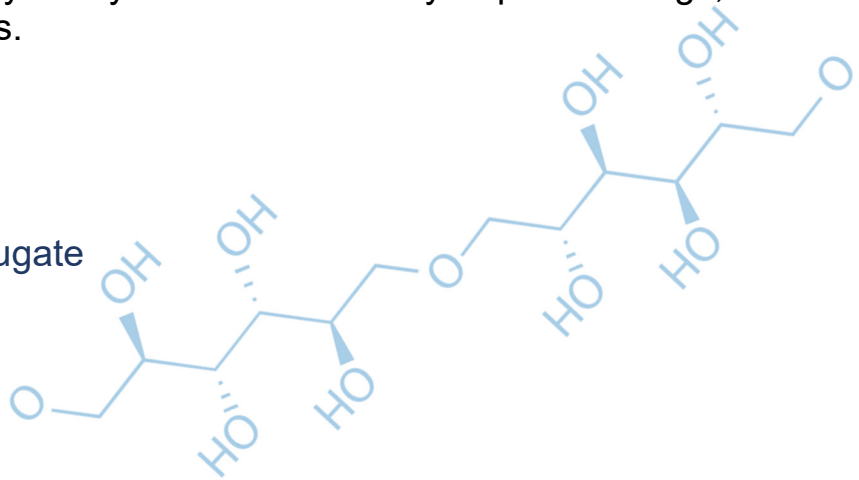
The AqueaTether™ platform can be applied to create new and better therapeutics across a broad range of drug molecules and treatment indications.

The AqueaTether™ platform can significantly accelerate the drug discovery process to deliver an optimized entity for development. It provides a broadly applicable approach to developing a new chemical entity (NCE) or new biological entity (NBE) with optimized drug profiles.

The AqueaTether™ platform offers a simple solution to complicated bioavailability, stability, and/or toxicity issues faced by many small-molecule hydrophobic drugs, as well as with large-molecule biologics.

AqueaTether™ Application Areas

- Antibody-Drug Conjugate
- Protein/Peptide/Oligo-Drug Conjugate
- Protein/Peptide Delivery
- Oligo/Gene Delivery
- Small Molecule Drug Delivery



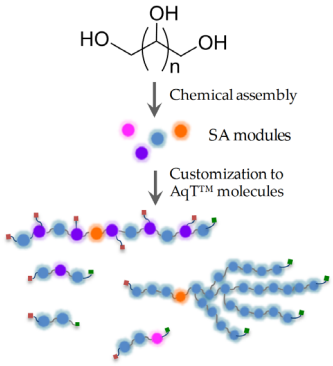
Contact us to see how the **AqueaTether™ platform** can potentially advance your program.

CellMosaic™

CellMosaic, Inc.
10A Roessler Road
Woburn, MA 01801
USA

Phone: 781-463-0002
Fax: 781-998-4694Email: info@cellmosaic.com
www.cellmosaic.com
www.aqttherapeutics.com

AqT™ linkers are the most customizable molecules in development due to the versatile nature of sugar alcohol monomers and the modular approach of our chemistry



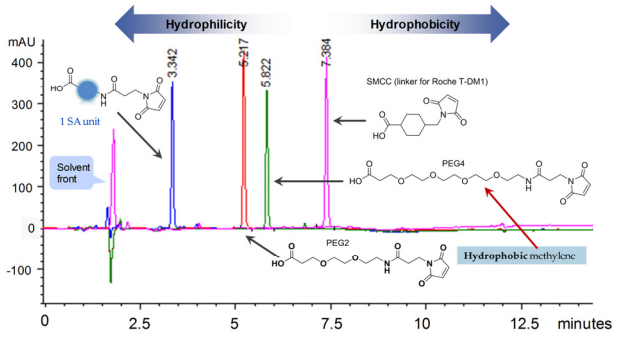
Modularity

Linker length, size and MW
Linkage chemistry
Loading capacity
Biodegradability
Molecule architecture

Translates into

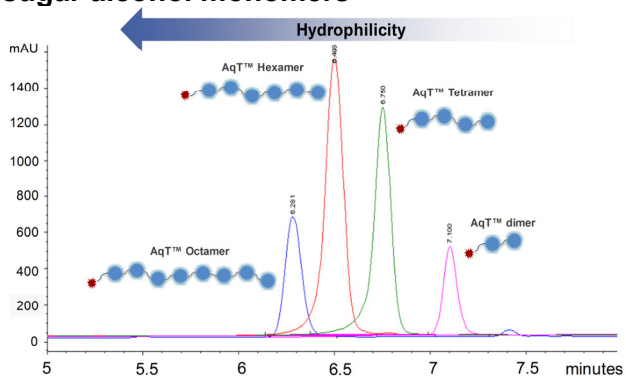
Better water solubility
Less protein precipitation/aggregation
Lower toxicity

AqT™ linkers are by far the most hydrophilic molecules in development



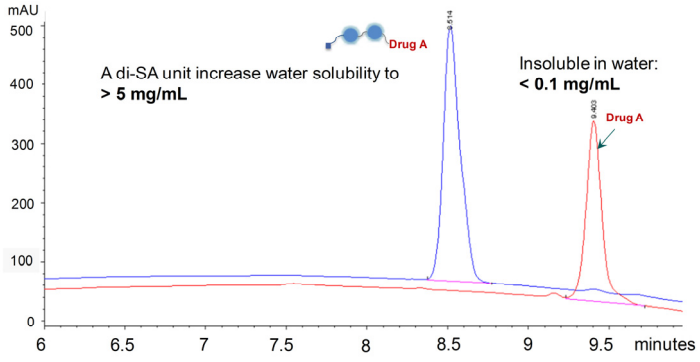
C18 HPLC analysis of AqT™ linker and other commercial linkers

The hydrophilicity of AqT™ linkers can be easily tuned by increasing the number of sugar alcohol monomers



C18 HPLC analysis of mono-dispersed AqT™ molecules of various SA units (Shallow Gradient)

AqT™ molecules can be used to increase the water solubility of any drug molecule



C18 HPLC analysis of a hydrophobic drug before and after a di-SA unit AqT™-linker labeling

Example: AqT™ linker greatly improves the water solubility and potency of SN38-labeled ADC

Table 1: Comparing the aggregation of the ADC reaction using SN38-acid with classical linker (SN38-acid) and SN38-acid with AqT linker (AqT™-SN38-acid).

Sample	Aggregation During Reaction (Based on SEC HPLC Data)
Antibody alone	3.5%
ADC Reaction with 16 Equiv. of AqT™-SN38-acid after overnight	18.1%
ADC Reaction with 16 Equiv. of SN38-acid after overnight	78.8%

Table 2: Comparing the cell killing effect of ADC labeled either with SN38-acid or AqT™-SN38-acid (DAR: 2-3). A great toxicity increase was obtained for AqT™-SN38-ADC.

Cell lines	IC50 (pM)			Increased toxicity (AqT™ vs classical linker)
	N38-ADC	AqT™-SN38-ADC	MMAE-ADC	
NCI-H1975	19529	8373	102.5	2.3
NCI-H226	8302	1142	N/A	7.5
A549	53594	788	N/A	68.0
PC9	35874	2584	205.4	7.0
	18183	788	N/A	3.6

CellMosaic™

CellMosaic, Inc.
10A Roessler Road
Woburn, MA 01801
USA

Phone: 781-463-0002
Fax: 781-998-4694Email: info@cellmosaic.com
www.cellmosaic.com
www.aqttherapeutics.com