POSTECH

Development of Therapeutic and Diagnostic Applications Using Ultrastable Supramolecular Interactions between Cucurbiturils and Their Binding Partners

Executive Summary

Dr. Kimoon Kim, a professor of Postech, has researched supramolecular chemistry using cucurbituril and developed cucurbit[n]uril (CB[n], n=5-10) and functionalized CB[n] with excellent quality, anticancer agent comprising CB[n] and pharmaceutical compound, cucurbituril-based drug delivery vehicles and platforms for detection, immobilization or purification of biomolecules.

The Postech intends to enter into a technology transfer or licensing transaction with regard to use of cucurbituril technology.

Cucurbituril technology has a wide scope such as household and environmental applications, drug delivery, non-covalent binding pair system, platform for biochips, biosensors and chromatography.

Industry Sector: Human Health/ Diagnostics/ Biomaterials(Drug delivery)

Therapeutic Target: N/A

State of Development: early stage

Key Technology Highlights

□ **Anticancer agent comprising Cucurbituril and pharmaceutical compound**

The pharmaceutical composition can prevent effective components from being biologically degraded *in vivo* and can exhibit continuous drug effect for a long time just by a single dosage by controlling the release time of the platinum complex once it reaches target tumor cells.

□ **Cucurbituril-based Drug-delivery vehicles**

Liposomes, capsules, or nanoparticles based on functionalized CB[n] can be easily prepared and decorated with imaging or targeting agents using supramolecular interaction between CB[n] and the binding partners. These vehicles can deliver various drugs with high efficiency in target-specific manner.

□ **Platforms for detection, immobilization, or purification of biomolecules**

Highly selective and ultrastable supramolecular interaction between CB[n] and their binding partners make it possible to detect, immobilize, or purify biomolecules such as proteins or nucleic acids.

■ IP Owner Summary

Pohang University of Science & Technology (POSTECH)

■ Personal Description of Researcher

□ **Name:** Kimoon Kim, Ph.D

□ **Present Position:**
Distinguished University Professor
Director, Center for Smart Supramolecules

□ **Major:**
Inorganic Chemistry
Supramolecular Chemistry

□ **Research interest.:**
Metal organic porous materials and supramolecules

□ **Office address:**
Department of Chemistry, POSTECH, San 31, Hyojadong, Pohang, 790-784, Korea

■ Market Feasibility

□ **Korean and Global market size:**

▹ US market for drug delivery system was USD 80.2 billion in 2007

▹ Global market for drug delivery systems was USD 134.3 billion in 2008

□ **Korean and Global market opportunity**

Global market for a representative macrocycle (cyclodextrin) was USD 4 billion in 2000

■ Trend & Partnership

□ **Future outlook and trends related to technology:**

This technology can provide novel materials for therapeutics, cosmetics, diagnosis, bioresearch and pharmaceutical research

□ **Technology Transfer and Commercialization conditions:**

Either licensee or co-development partner should be vertically integrated company with full development and commercialization capabilities for at least the proposed territories of interest. Expected terms of licensing agreement will be similar to industry practice of involving upfront, development and regulatory milestones, and royalty payments.

□ **Type of business relationship sought**

Development collaboration, or non-exclusive or exclusive licensing agreement (both worldwide and regional) can be available

Technology Overview

■ Technology Platform

The core technology of Postech is to provide cucurbit[n]uril (CB[n], n=5-10) and functionalized CB[n] with excellent quality and applied it in various fields.

■ Background and unmet needs

Cucurbit[n]uril (CB[n], n = 5-10) is a family of macrocyclic compounds comprising *n* glycoluril units. The pumpkin-shaped CB molecules have a hydrophobic cavity and two identical carbonyl-laced portals. While the hydrophobic interior provides a potential inclusion site for nonpolar molecules, the polar ureido carbonyl groups at the portals allow CB[n] to bind ions and molecules through charge-dipole and hydrogen bonding interactions. We and others recently reported that CB[7] binds ferrocene derivatives with an exceptionally high binding constant (K ~ 10^{15} M^{-1}) and good specificity in aqueous solution. The unique structure and recognition properties make CB[n] attractive not only as a synthetic receptor but also as a building block for the construction of supramolecular architectures. Furthermore, a direct functionalization method of CB[n] allowed synthesizing a wide variety of tailor-made CB derivatives to study many applications. Ion channels, vesicles, polymers, nanomaterials, ion selective electrodes incorporating CB[n], and CB-immobilized solid surfaces and silica gel have been reported and numerous other applications are being explored.

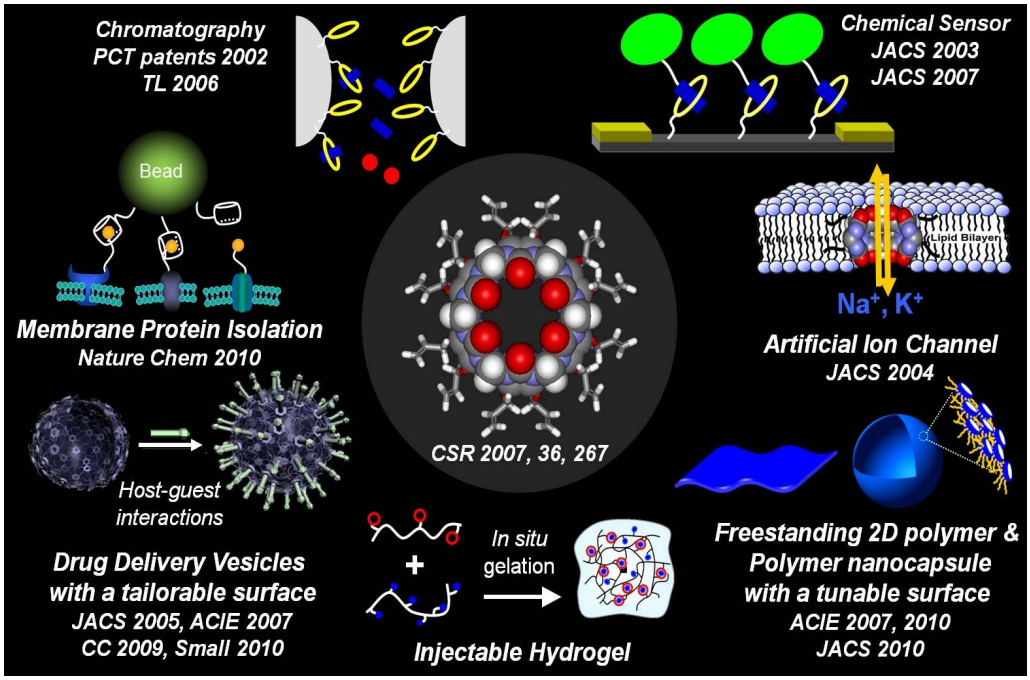

Fig. 1. Applications of functionalized cucurbiturils (developed by Kimoon Kim and coworkers at POSTECH)

■ **Discovery and Achievements**

Our research on CB[n] has many useful applications. For example, CB[n] can encapsulate a number of platinum-containing anticancer drugs, thus increasing their bioavailability and reducing their side effects. Nanometer-sized vesicles (*JACS* 2005), capsules (*ACIE* 2007), and nanoparticles (*ChemComm* 2009) made of CB[6] derivatives are potentially useful in delivering drugs to specific targeted cells and tissues to enhance the efficacy of the drugs while minimizing the side effects. The synthetic ligand-receptor pair with ultrahigh binding affinity (*PNAS* 2007) which can be used as a “glue” in many chemical and biological applications may contribute to accurate and fast diagnosis. CB[n] and their derivatives to be useful in waste water treatment, odor removal, release of fragrance, separation of important bioactive molecules and many other nano- and biotechnological areas.

Patents and Publications

Table 1. List of Patents for cucurbituril Technology

Country	Patent, Publication or Appln. No.	Status	Description
US	6365734, 6639069, 7160466	Granted	Cucurbituril derivatives, their preparation methods and uses (Material, Method, Use)
US	7388099	Granted	Hydroxycucurbituril derivatives, their preparation methods and uses
US	7459471	Granted	Inclusion compound comprising cucurbituril derivatives as host molecule and pharmaceutical composition comprising the same
US	7504029	Granted	Silica gel bonded with cucurbiturils
Korea	10-0545583	Granted	Cucurbituril derivative-bonded solid substrate and biochip using the same
Korea	10-0554156	Granted	Nano-particles comprising cucurbituril derivatives, pharmaceutical composition containing the same, and process for the preparation thereof
US	7520982	Granted	Cucurbituril-containing polymer, stationary phase and column using the same
US	7781050	Granted	Ultrathin polymer film using cucurbituril derivative and method of forming the same
Korea	10-0670948	Granted	A bundle of carbohydrates covalently bonded to single molecule of cucurbituril derivative
PCT	PCT/KR2006/001482	Pending	Polymer capsule and process for the preparation thereof
US	7479254	Granted	A compound used as a stationary phase of an affinity chromatography for purifying cucurbituril and a method of purifying cucurbituril using the compound
PCT	PCT/KR2006/001096	Pending	Stationary phase and column cucurbituril bonded silica gel, and separation method of taxol using the column
PCT	PCT/KR2006/000841	Pending	Cucurbituril added cigarettes and manufacturing method thereof
PCT	PCT/KR2008/001887	Pending	Liposome sensitive to pH or reductive condition and processes for the preparation thereof
PCT	PCT/KR2009/001947	Pending	The method of separating and purifying cellular components using non-covalent bond between a cucurbituril derivative and a guest compound and an apparatus using the same

Table 2. List of Selected Publications for cucurbituril Technology

No.	Author	Journal	Title
1	S. Y. Jon, N. Selvapalam, D. H. Oh, J.- K. Kang, S.-Y. Kim, Y. J. Jeon, J. W. Lee, and K. Kim	*J. Am. Chem. Soc.*, **2003**, *125*, 10186-10187	Facile Synthesis of Cucurbit[n]uril Derivatives via Direct Functionalization: Expanding Utilization of Cucurbit[n]uril
2	Y. J. Jeon, S.-Y. Kim, Y. H. Ko, S. Sakamoto, K. Yamaguchib and K, Kim	*Org. Biomol. Chem.*,, **2005**, *3*, 2122-2125	Novel molecular drug carrier: encapsulation of oxaliplatin in cucurbit[7]uril and its effects on stability and reactivity of the drug
3	K Kim, N. Selvapalam, Y. H. Ko, K. M. Park, D. Kim and J. Kim	*Chem. Soc. Rev.,* **2007**, *36*, 267–279	Functionalized cucurbiturils and their applications
4	I. Hwang, K. Baek, M. Jung, Y. Kim, K. M. Park, D. -W. Lee, N. Selvapalam, and K. Kim	*J. Am. Chem. Soc.*, **2007**, *129*, 4170-4171	Noncovalent Immobilization of Proteins on a Solid Surface by Cucurbit[7]uril-Ferrocenemethylammonium Pair, a Potential Replacement of Biotin-Avidin Pair
5	D. Kim, E. Kim, J. Kim, K. M. Park, K. Baek, M. Jung, Y. H. Ko, W. Sung, H. S. Kim, J. H. Suh, C. G. Park, O. S. Na, D.-k. Lee, K. E. Lee, S. S. Han and K. Kim	*Angew. Chem. Int. Ed.*, **2007**, *46*, 3471-3474	Direct Synthesis of Polymer Nanocapsules with a Noncovalently Tailorable Surface
6	M. V. Rekharsky, T. Mori, C. Yang, Y. H. Ko, N. Selvapalam, H. Kim, D. Sobransingh,A. E. Kaifer, S. Liu, L. Isaacs, W. Chen, S. Moghaddam, M. K. Gilson, K. Kim, and Y. Inoue	*Proc. Natl. Acad. Sci.*, **2007**, *104*, 20737–20742	A synthetic host-guest system achieves avidin-biotin affinity by overcoming enthalpy–entropy compensation
7	K. M. Park, K. Suh, H. Jung, D.-W. Lee, Y. Ahn, J. Kim, K. Baek and K. Kim	*Chem. Commun.*, **2009**, 71-73	Cucurbituril-based nanoparticles: a new efficient vehicle for targeted intracellular delivery of hydrophobic drugs
8	E. Kim, J. Lee, D. Kim, K. E. Lee, S. S. Han, N. Lim, J. Kang, C. G. Park and K. Kim	*Chem. Commun.*, **2009,** 1472 –1474	Solvent-responsive polymer nanocapsules with controlled permeability: encapsulation and release of a fluorescent dye by swelling and deswelling
9	E. Kim, D. Kim, H. Jung, J. Lee, S. Paul, N. Selvapalam, Y. Yang, N, Lim, C. G. Park, and K. Kim	*Angew. Chem. Int. Ed.,* **2010**, *49*, 4405 –4408	Facile, Template-Free Synthesis of Stimuli-Responsive Polymer Nanocapsules for Targeted Drug Delivery
10	K. M. Park, D. W. Lee, B. Sarkar, H. Jung, J. Kim, Y. H. Ko, K. E. Lee, H. Jeon, and K. Kim	*Small*, **2010**, *6*, 1430-1441	Reduction-Sensitive, Robust Vesicles with a Noncovalently Modifiable Surface as a Multifunctional Drug-Delivery Platform
11	J. Y. Kim, Y. J. Ahn, K. M. Park, D. W. Lee, and K. Kim	*Chem. Eur. J.*, **2010**, *16,* 12168–12173	Glyco-pseudopolyrotaxanes: Carbohydrate Wheels Threaded on a Polymer String and Their Inhibition of Bacterial Adhesion
12	D. W. Lee, K. M. Park, M. Banerjee, S. H. Ha, T. Lee, K. Suh, S. Paul, H. Jung, J. Kim, N. Selvapalam, S. H. Ryu and K. Kim	*Nat. Chem.* in press	Supramolecular fishing for plasma membrane proteins using an ultrastable synthetic host–guest binding pair