Coordination Polymer Particles for New Generation of Drug Delivery

Ji Li Literature Seminar November 5 2013

Coordination polymer is a coordination compound with repeating coordination entities extending in 1, 2 or 3 dimensions.[1] In the 1960s, John C. Bailar and his research group contributed to the first series of approaches to build up inorganic polymers based on coordination bond.[2] Although people have long been interested in their crystalline network form, well known as Metal-Organic Framework (MOF), it was only until 2005 that the first examples of nano- or microscale coordination polymers particles (CPPs) be demonstrated.[3] Chad Mirkin and colleagues discovered the formation of micro- or nanoparticles from connecting metal ions (Zn^{2+}, Cu^{2+}, Ni^{2+}) with carboxylate functionalized binaphthyl bis-metallo-tridentate Schiff base (BMSB) building blocks. Adding an initiate solvent to the aqueous mixture of the cations and ligands precipitated the particles followed by centrifuge purification. (Fig. 1) [3a]

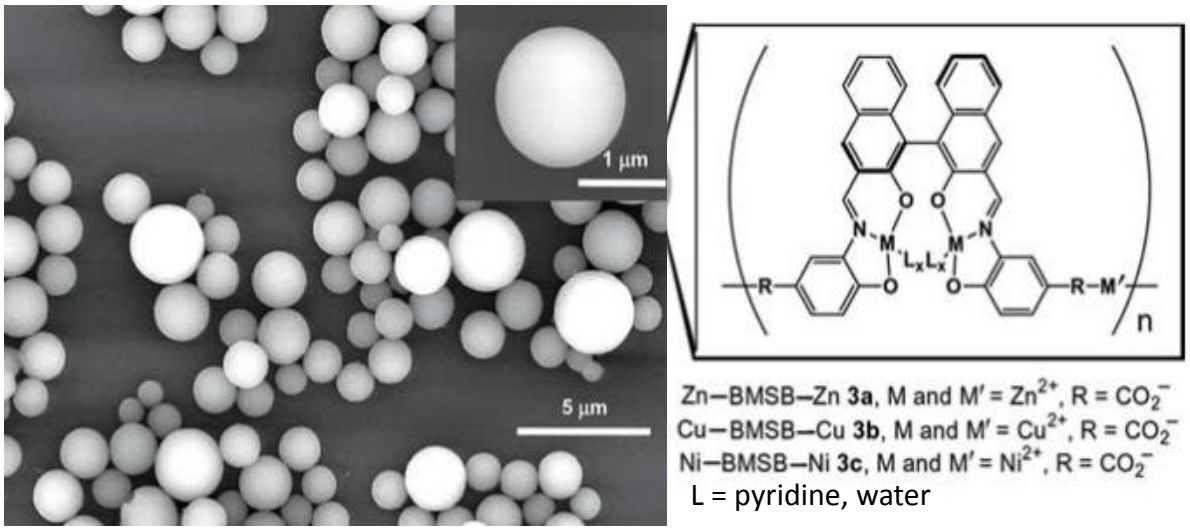

Figure 1. SEM image of the coordination polymer particles and the composition

Drug delivery is the approach to transport therapeutic agents in the body so that higher local concentration of the drug at the target of interest can be achieved. The development of the nanotechnology has facilitated the emerging of nanocarriers of various kinds to selectively deliver the drugs to the target, tumor tissue for instance, and release the drugs in a controlled manner.[4] Although many systems such as liposome, polymer particle, dendrimer and inorganic particles have been demonstrated for their capability of loading and releasing drugs, each of the system has weakness to impede the broad application of nanomedicines.[5] CPPs as an alternative to other nanocarriers process many advantages due to the nature of the coordination polymer such as high tailorability and diversity. In recent five years, many work have been done in this field to show the potential of CPPs for future biomedical therapeutic applications.

The incorporation of the therapeutic agents into the CPP mainly falls into two categories, encapsulation of the drug into the interspaces of CPP or applying drug or pro-drug as the building block for the polymer. Imaz et al demonstrated the capability of the CPP formed from

Zn^{2+} and 1,4-bis (imidazole-1-ylmethyl) benzene for encapsulating various kinds of functional moieties ranging from iron oxide nanoparticles, quantum dots and fluorescent dyes.[6] Doxorubicin was also successfully encapsulated in the CPP and the release profile was tested, showing a fast release of around 80% at hours attributed to the diffusion of the drugs.[7] Horcajada et al developed a group of crystalline CPP from biocompatible Fe (III) and carboxylate ligands to encapsulate various anti-cancer drug and anti-AIDS drugs, showing the generality of this approach and its promising application in theranostic while drug delivery and magnetic resonance imaging (MRI) are performed simultaneously.[8]

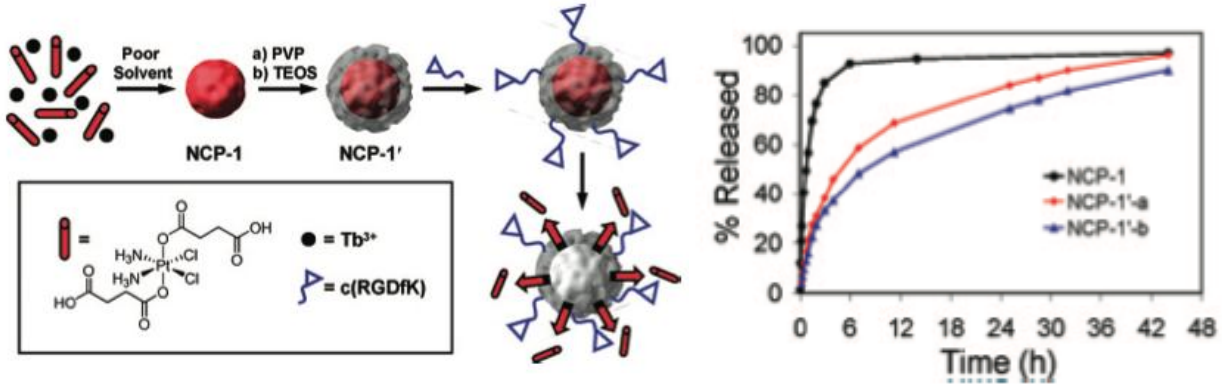

Figure 2. Schematic illustration of the Pt based pro-drug building block strategy (left) and release profile of particles with different thickness of silica coating

Wenbin Lin and colleagues developed the first example of applying Pt based pro-drugs as building blocks for CPP based delivery applying Tb3+ ions and disuccinato-cisplatin (DSCP) as the bridging ligand.[9] Surface modification of the CPP with silica was applied in order to control the release rate of the therapeutic agents. In vitro cytotoxicity was also performed with targeting agent functionalized CPP and show IC_{50} of 9.7 μM and 11.9 μM respectively for different silica thickness, comparable to the free cisplatin standard at 13.0 μM. The same group later performed lipid surface functionalization of Zn2+, Zr2+ and Gd3+ and Methotrexate (MTX) CPP, which facilitates the cellular uptake and thus shows better cytotoxicity.[10]

Recently, people have been making progress on the CPP drug delivery system mainly in two directions. One is the stimuli-responsive release of the therapeutic agents while the other is the combination with other nanomaterials. Xing et al developed the CPP system based on labile "metal-ligand" bond and "host-metal-ligand", the cleavage of which is triggered by acidic pH and thus fulfill the pH-responsive drug release.[11] The core-shell structure combined with a drug loading core and pH-responsive shell is also reported for higher stability and better targeting effect.[12] An example of the combination of CPP with other nanomaterials is the incorporation of CPP with gold nanorods. Well-defined core-shell structure can be shown and the light-induced drug release could be achieved, as demonstrated by Khaletskaya.[13]

Although the research on the CPP for drug delivery is still in an early stage, the recent findings suggest the bright future of the application of CPP to biomedical applications. The design of a general vehicle structure with high stability, targeting effect and controlled release profile still lies on the future direction. With these critical problem solved and more in vivo behavior tested, CPP will be the candidate of new generation of smart drug delivery system.

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