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論　文　内　容　要　旨

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学位論文題目	Water-Solubilization by Using Symmetrically Branched Oligoglycerol Trimers （対称分岐型オリゴグリセロール三量体を用いた水溶性化研究）

Branched glycerol trimer (BGL003) and heptamer (BGL007) were originally developed by our research group as a water-solubilizing fragment. BGL003 and BGL007 have strong water-affinity due to the presence of four and eight primary hydroxy groups, respectively. From the literature surveyed, previously BGL was used in improving the water-solubility of several hydrophobic medicinal small molecules and thermal stability of artificial protein by covalent conjugation. In my doctoral research work, BGL003 has been covalently connected with several lipophilic molecules to increase the hydrophilicity.

In my first project, Alkanethiols have been chemically modified by BGL003 to develop a lipophilic-thiolate-chemisorbed “Self-assembled Monolayers” (SAM) on metal in an aqueous solution. The most popular method for depositing a molecular layer on expensive metal surfaces is a chemisorption of organosulfur molecules such as alkanethiols via the formation of SAMs. Due to the high lipophilicity of alkanethiol, use of organic solvent has been unavoidable until now. Here, I have designed and synthesized long chain alkanethiol-BGL derivatives which are water soluble. For this project, six long chain thiols have been selected for thiol probe and among these octadecanethiol (ODT) used as a representative one. ODT has been connected with BGL003 through succinyl residue by thioester linkage formation and converted lipophilic ODT to water-soluble derivative (ODT–Su–BGL). This octadecanethiol derivative was applied for novel transition metal coating in water and the thioester linkage was probably activated by metal itself to cleave sulfur–carbonyl bond to afford octadecanethiolate residue (RS^-). In fact, the resulting property of the silver or gold plate by treating ODT (standard method) was almost the same as by treating ODT–Su–BGL in water. Finally, an environmentally friendly coating method has been developed from this project.

In the second project, a couple of BGL003 with new apex was developed. Using *N*-acyl tyrosine methylamide as a smallest model of peptides and SN38 as an antineoplastic drug, the new BGL003 was connected with side chain of tyrosine and A-ring of SN38, respectively, via one additional linker molecule. Paclitaxel and docetaxel are also a chemotherapy medication used to treat a number of types of cancer. These drugs are also given by slow injection due to poorly water-soluble. Here, another new BGL003 has been conjugated with de-(N-benzoyl)-paclitaxel and de-(N-Boc)-docetaxel. I believe these BGL003 modified drugs will be more hydrophilicity and increase absorption amount in the human body. The efficiency (*in vitro and in vivo*) of this modified drugs will be tested later on.