Synthesis and Structural Characterization of Magnesium Drug Complexes: Efficient Initiators for Forming Polylactide–Drug Conjugates.

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Over the recent decades there has been increasing interest in the conjugation of polymers with drugs to improve and modify their biopharmaceutical properties. Indeed, from a human health care perspective, numerous polymer-drug conjugates have been investigated. The possibility of linking a bioactive molecule to a macromolecular chain to make polymeric conjugated systems is applicable not only in drug delivery but also in fields such as tissue engineering, biosensors, affinity separations, enzymatic processes, and cell cultures. In studies related to these, popular synthetic polymers such as biodegradable polymers,[1] especially with polylactide (PLA).

Topic of the lecture includes a new, simple, and efficient strategy for preparing a well-defined magnesium–drug initiator and their application in polymerization of L-LA to allow the formulation of PLA–drug conjugates with end-capped VenlO and PriO groups. The drugs *pridinolum* (PriOH = 1,1-diphenyl-3-(1-piperidinyl)-1propanol) and *venlafaxinum* (VenlOH = (RS)-1-[2-dimethylamino-1-(4-methoxyphenyl)ethyl]cyclohexanol) are used as a muscle contraction agents and antidepressants, respectively and may be used as versatile N,O-bifunctional supporting ligands as the initiating group for the synthesis of PLA–drug conjugates. As a result , we received new dimeric drug-magnesium $[Mg(\mu,\eta^2\text{-OPri})Bu]_2$ (**1**) and $[Mg(\mu,\eta^2\text{-VenlO})Bu]_2$ (**2**), $[Mg(\mu,\eta^2\text{-OVenl})(\eta^1\text{-OPri})]_2$ (**3**), $[Mg(\mu,\eta^2\text{-OPri})(\eta^1\text{-OPri})]_2$ (**4**), and $[Mg(\mu,\eta^2\text{-OVenl})(\eta^1\text{-OVenl})]_2$ (**5**) compounds in crystalline form.[2] Moreover, we found that synthesized complexes **1-5** are highly active initiators of the ROP of L-LA to give polymers terminated by a covalently attached drug molecule through ester linkers. These have potential use in drug delivery and controlled-release applications.

Reference:

1) Petrus, R.; Bykowski, D.; Sobota, P.; *ACS Catal.* **2016**, 6, 5222–5235.
2) Han,T; Petrus, R.; Bykowski, D.; Jerzykiewicz, L.; Sobota, P.; *Organometallics,* **2015**, 34, 4871–4880.

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