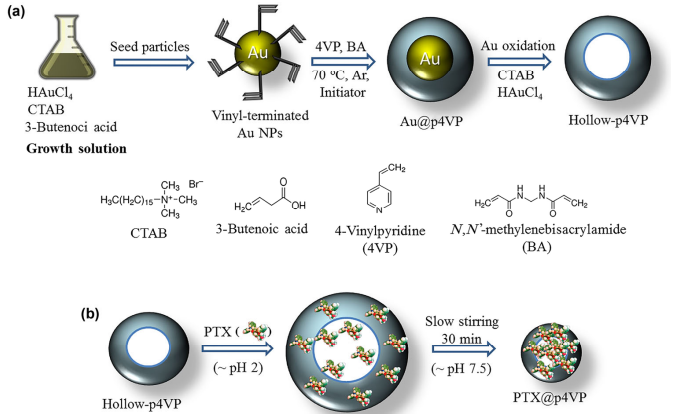
Hollow polymeric nanoparticles to enhance drug chemotherapeutic efficacy

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Abstract (300 word limit)

Paclitaxel (PTX), one of the most effective drugs for the treatment of breast and lung cancer, is limited by its severe side effects and low tumor selectivity. We carried out pH responsive hollow-poly(4-vinylpyridine) (hollow-p4VP) and Au (Au@p4VP) nanoparticles (NPs) that have been used to generate PTX@p4VP NPs, employing a technique in which a gold core in the center of the NP is further oxidized to produce the hollow structure into which PTX molecules can be incorporated. The hollow-p4VP NPs exhibit good physicochemical properties and displayed excellent biocompatibility when tested on blood (no hemolysis) and cell cultures (no cytotoxicity). Moreover, mean diameter, ranging from 150 to 57 nm, can be accurately controlled upon varying the monomer concentration at synthesis. Interestingly, PTX@p4VP NPs significantly increased PTX cytotoxicity in human lung (A-549) and breast (MCF-7) cancer cells with a significant reduction of PTX IC_{50} (from 5.9 to 3.6 nM in A-549 and from 13.75 to 4.71 nM in MCF-7). In addition, PTX@p4VP caused a decrease in volume of A-549 and MCF-7 multicellular tumor spheroids (MTS), an *in vitro* system that mimics *in vivo* tumors, in comparison to free PTX. This increased antitumoral activity is accompanied by efficient cell internalization and increased apoptosis, especially in lung cancer MTS. Our results offer the first evidence that hollow-p4VP NPs can improve the antitumoral activity of PTX. This system can be used as a new nanoplatform to overcome the limitations of current breast and lung cancer treatments. The good results obtained for PTX allowed us to extend the use the colloidal hybrid system to doxorubicin (Dox) and 5-fluorouracil (5Fu). Here we present a complete characterization of PTX@p4VP NPs together with our preliminary results for these two anticancer drugs included into hollow polymeric systems.

Image



Recent Publications (minimum 5)

1. Contreras-Cáceres R, Leiva MC, Ortiz R, Díaz A, Perazzoli G, Casado-Rodríguez MA, Melguizo C, Baeyens JM, López-Romero JM, Prados J (2017) Hollow-p4VP Nanoparticles Loading Paclitaxel to Enhance Drug Chemotherapeutic Efficacy in Lung and Breast Cancer Cell Lines. Nano Res. 10:856-875.
2. Benavente J, García ME, Urbano N, López-Romero JM, Contreras-Cáceres RC, Casado-Rodríguez MA, Moscoso A, Hierrezuelo J, (2017) Inclusion of silver nanoparticles for improving regenerated cellulose membrane performance and reduction of biofouling. Int. J. of Biolog. Macromol. 103:758-763.
3. Leiva MC, Ortiz R, Contreras-Cáceres R, Perazzoli G, Mayevych I, López-Romero JM, Sarabia F, Baeyens JM, Melguizo C, Prados J (2017) Tripalmitin nanoparticle formulations significantly enhance paclitaxel antitumor activity in breast and lung cancer cells in vitro. Scientific Reports 1: Art. Number: 13506.
4. Clara-Rahola J, Moscoso A, Ruiz-Muelle AB, Laurenti M, Formanek P; López-Romero JM; Fernandez JM, Diaz JF, Rubio-Retama JM; Fery A (2018) Au@p4VP core@shell pH-Sensitive Nanocomposites Suitable for Drug Entrapment. J. Colloid and Interface Sci. 514: 704-714.
5. Kuttner C, Mayer M, Dulle M, Moscoso A, López-Romero JM, Förster JM, Fery A, Perez-Juste J, Contreras-Cáceres R (2018) Seeded Growth Synthesis of Gold Nanotriangles: Size Control, SAXS Analysis, and SERS Performance. ACS Appl. Mat. & Interfaces 10:11158-11163.



Biography (150 word limit)

JM López-Romero is professor of Organic Chemistry at the University of Málaga (Spain). *Postdoctoral studies were carried out at the University Pierre et Marie Curie (Dr. Max Malacria, Paris VI, France) and University of Houston (Dr. Chengzhi Cai, USA). He is founder and director of Icon Nanotech S.L., a Spanish Spin-Off company dedicated to nanotechnology and natural products. He has published more than 60 papers in reputed journals. Research interest includes synthesis of natural products, macromolecules and nanoparticles, all of them with applications in nanomedicine, cosmetics and in surface nanostructuration.*

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