Novel Palladium-Graphene Catalysts Improve Pharmaceutical Processing

Pharmaceutical companies use a variety of metal catalysts to produce active pharmaceutical ingredients (APIs). One of the most widely used catalytic reactions in commercial operation is the Suzuki cross-coupling reaction, which can produce high-volume drugs such as the anti-hypertension drug losartan. These reactions traditionally employ homogeneous palladium catalysts, which often require extensive purification to separate the catalyst from the product.

Heterogeneous, or solid-supported, catalysts have supports that serve mainly as relatively large platforms for the nanoscale palladium catalysts, and the supports can be easily separated out. Pharmaceutical companies are developing heterogeneous catalysts to reduce overall API manufacturing costs. However, the challenge in developing solid-supported catalysts is preventing the leaching of palladium from the solid surface to avoid product contamination.

Researchers at Virginia Commonwealth Univ. in Richmond, VA, and at the Univ. of South Carolina in Columbia, SC, have developed an innovative method to produce extremely active heterogeneous palladium catalysts with precise control of palladium loading. This new method combines strong electrostatic adsorption (SEA) metal deposition with microwave (MW) irradiation (SEA-MW) to produce these highly reactive catalysts.

In the SEA-MW process, scientists adjust the pH of an ionic palladium precursor solution to either protonate or deprotonate the graphene surface. This directs the graphene support to uptake, or electrostatically adsorb, the ionic palladium precursor onto its surface. Then, a solventless MW irradiation treatment simultaneously forms palladium nanoparticles (1–3 nm) and creates holes or defects in the graphene sheet. Computational and experimental research shows that these holes, or defects, in the graphene enhance catalytic activity and palladium binding. In addition, the research shows the graphene material effectively serves as a charge reservoir and actively assists in charge donation and acceptance steps throughout the Suzuki reaction. These results strongly suggest that the graphene materials act as a solid-state ligand that can assist in catalysis and still be easily separated out.

The SEA-MW method forms ultrasmall palladium nanoparticles and clusters. Both forms are supported by graphene defects, via three scenarios:

- Pre-existing graphene defects or holes support the palladium nanoparticles and clusters.
- Protonated or deprotonated oxygen functional groups take up ionic palladium complexes. Microwave irradiation then simultaneously removes carbon and oxygen (as CO or CO_2) to create graphene defects and form palladium nanoparticles. The close proximity of the recently formed nanoparticles and graphene defect allows the nanoparticles to bind strongly to the graphene defect.
- Graphene's protonated pi bonds (in the middle of the honeycomb-like lattice of the aromatic rings, away from oxygen and away from edges) take up the ionic palladium complexes. During the microwave irradiation step, the palladium very strongly absorbs the energy and grows hot enough to directly burn, or pyrolyze, holes in the graphene support.

The SEA-MW catalysts exhibit catalytic activities 16 times higher than commercially available palladium-on-carbon catalysts. This improvement could allow manufacturers to reduce the use of expensive palladium and lower the overall price of the pharmaceutical drug. In addition, the process does not require solvents or reducing agents. Other advantages of the SEA-MW method include the use of low MW powers (50–150 W), short reaction times (10 min), and atmospheric reaction conditions. Also, metal contamination is minimized because the palladium nanoclusters are tightly bound to the relatively large graphene surfaces, which can be easily filtered from the reaction mixture.

Although the SEA-MW method holds great promise in pharmaceutical catalysis, the cost of graphene materials can be a concern. However, this method has been demonstrated on four different types of graphene materials, including graphene nanoplatelets (GNPs), which are significantly more cost-effective (< $1/g) than other graphene materials. The researchers — who are part of the Center for Rational Catalyst Synthesis (CeRCaS), an Industry-University Cooperative Research Center (IUCRC) funded by the National Science Foundation (NSF) — are currently working with the CeRCaS member companies (Biogen, Boehringer Ingelheim, and ThalesNano) to commercialize these materials.

Richard Jones, an executive with ThalesNano, says, "We have found these graphene-supported palladium catalysts to possess remarkable catalytic activity, and we are currently evaluating how they can be integrated into our product line." CEP

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