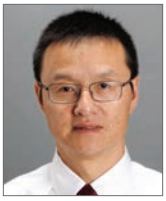
Controlled Release | Targeted Delivery | Solubility Enhancement

# BIODEGRADABLE COLLOIDAL CARRIERS
## IN DRUG DELIVERY APPLICATIONS




Bin Wu, Theresa Logan
Phosphorex, Inc.
Hopkinton, MA USA
bin.wu@phosphorex.com and tlogan@phosphorex.com

## Introduction

Colloidal carriers are particles or vesicles of nanometer to micron size that facilitate drug delivery. Common colloidal carrier systems include liposomes, polymeric microspheres and nanoparticles, nanocrystals, and microemulsions. Colloidal carriers can be used to improve the therapeutic index of APIs by transporting loaded drugs to the target site and modifying their distribution within the body. Furthermore, colloidal carriers can alter the pharmacokinetics of drug molecules, increase efficacy, reduce toxicity, and provide controlled and sustained release.

## Polymeric Microspheres

Polymeric microsphere drug carriers are spherical particles in the size range of several to hundreds of microns that can protect unstable drugs pre- and post-administration. Microspheres have the ability to release a drug continuously over time,[1] thereby providing a prolonged therapeutic effect and reducing the dosing frequency. In addition to controlled release, microspheres allow for the targeted drug delivery of potent drugs at reduced concentrations, thereby minimizing systemic exposure and adverse side effects. Finally, polymeric microspheres facilitate manipulation of *in vivo* behavior, pharmacokinetic profile, tissue distribution, and cellular interaction of the drug.[2]

Microspheres are typically comprised of biodegradable polymers such as poly(lactide-co-glycolide) (PLGA), polylactic acid (PAA), polylactide (PLA), and polycaprolactone (PCL). These polymers degrade *in vivo* by hydrolysis of their ester backbone into non-toxic products, which are excreted by the kidneys or eliminated as $CO_2$ and water through biochemical pathways. PLGA microspheres have been widely used to encapsulate drug molecules and have been used as long-acting, sustained-release pharmaceutical formulations. There are several drug-loaded PLGA microspheres approved by the FDA and marketed for clinical use. For example, depot products, such as luprolide acetate microspheres used for the treatment of prostate cancer and endometriosis, can be subcutaneously administered at 1-month, 3-month, or 6-month intervals. When drug-loaded PLGA microspheres are administered, the PLGA polymer starts to degrade *in vivo*, and as it degrades the drug molecules are gradually released from the microspheres. The drug release rate can be modulated by the selection of the type of PLGA polymer and by adjusting the encapsulation process. For example, the following parameters can affect the drug release profile:

- The ratio of lactide to glycolide (L/G ratio) in the PLGA polymers; e.g., PLGA with an L/G ratio of 50:50 have the fastest drug release.
- The molecular weight or inherent viscosity of the PLGA polymer, where higher molecular weight provides slower drug release.
- The terminal group of the PLGA polymer, where carboxyl-terminated PLGA polymers offer faster drug release compared to ester-terminated PLGA.

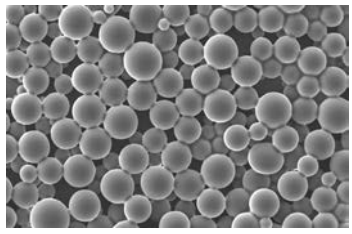


**Figure 1**. Image of API-loaded PLGA microspheres.

## Polymeric Nanoparticles

Polymeric nanoparticles (NP), either plain or drug loaded, are typically less than 1 micron in size. The use of API-loaded polymeric nanoparticles for intravenous administration is a promising approach for achieving the controlled release and site-specific delivery of drugs. The nanoparticle delivery system can be designed to maintain appropriate therapeutic concentration in the bloodstream (controlled release) or to target a specific cell type (e.g., bone marrow, blood cells). Various types of APIs, including small molecule drugs and biologic compounds, can be incorporated into PLGA polymer nanoparticles by either microencapsulation or surface conjugation. Nanoencapsulation can protect the API from early degradation, facilitate cell entry, and increase solubility and bioavailability.

The surface properties of intravenously injected particles are important factors determining *in vivo* organ distribution and fate. Furthermore, surface modification can be an effective approach to targeting specific