157g Engineering Shape of Polymeric Microparticles for Drug Delivery

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Nano- and microspheres injected into the body for drug delivery purposes are eventually cleared by phagocytosis. During phagocytosis, macrophages engulf their targets (particles) and internalize them via an actin-mediated process. Although polymeric spheres of various sizes ranging from a few tens of nanometers to several tens of microns have been used for drug delivery, very little attention has been paid to the role of shape of these particles in drug delivery. We hypothesize that the shape will influence the performance of these particles, most importantly their phagocytosis. To evaluate this hypothesis, we designed geometrically anisotropic polymeric microparticles and assessed their phagocytosis using alveolar macrophages. Twenty different particle geometries representing six distinct shapes were fabricated: spheres, prolate ellipsoids, oblate ellipsoids, elliptical disks, rectangular disks, and Saturn-shaped particles. Dimensions of these particles ranged from one hundred nanometers to thirty microns. Collectively, these particles possessed volumes, surface areas, curvatures, and maximum lengths that spanned several orders of magnitude.

We report that particle shape, more precisely local curvature at the point of attachment, plays a decisive role in phagocytosis, more so than particle size. This result challenges the theory that size primarily determines a particle's phagocytic fate. We report fundamental studies based on video microscopy and scanning electron microscopy that explain the interplay between the size and shape of particles in determining their phagocytic fate. We found that macrophages “sense” the local curvature of particles and make a decision whether or not initiate phagocytosis. Attachment of macrophages in regions of high local curvature makes particles most susceptible to initiation of internalization. Size (volume or length) primarily impacts completion of phagocytosis in cases where particle volume approaches or exceeds the cell volume. This revelation highlights the profound impact of particle shape on phagocytosis, a crucial step in particulate drug delivery. Such understanding will be extremely useful in the design of the next generation of particulate drug delivery systems.