Inhaled Micro- or Nanoparticles: Which are the Best for Intramacrophagic Antiinfectious Therapies?

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Intramacrophagic Anti-infectious therapies

Nanotechnology is a fascinating world that has provided and still provides sensational developments in many fields such as in pharmaceutics for diagnosis or drug and gene delivery to cells, tissues or organs. With regard to the latter, cell uptake of nanostructures (generally 1-100 nm) is usually much greater than that of microparticles in the range of 1-10 µm. Although the term “nano” remains of high impact, not always the nanosize is preferable to a microparticles in the range of 1-10 µm. Nevertheless, particle deposition onto the distal respiratory tract (breathability) is a prerogative of microsize particles in the aerodynamic size from 0.5 to 5 µm (but also 0.5-3, 0.5-2, or 3-6 µm ranges are referred) while particles smaller than 0.5 µm are mostly exhaled without deposition [3]. Contrary to this, particles larger than 2 or 5 µm, according to the data reported by the researchers, have a lower possibility of bypassing the upper airways. From the perspective of the AM endocytosis, the literature shows a wide view of dimensional conditions under which AM uptake would be subjected according to the size dictating endocytosis mechanism: phagocytosis (particularly 1-3 µm), macropinocytosis (0.2-10 µm), or pinocytosis (<0.2 µm).

It is essential to underline that cell-particle interactions are modulated also by other physico-chemical properties as well as cell-specific parameters such as macrophage type, i.e. the tissues where macrophage reside. For instance, some authors refer optimal sizes of the particles for the phagocytosis uptake by AM in the range between 3 µm and 6 µm, but those by peritoneal macrophages and peripheral blood mononuclear cells from 0.3 µm to 1.1 µm [1].

However, the impact of particle size on both passive and active uptake is considered a key parameter with a tendency to assume and demonstrate that nanoparticles largely escape uptake by AM. Indeed, although endocytic mechanisms can involve nanoparticles, the actual amounts taken up should be assayed before a possible consideration. For example, 0.1% of the inhaled dose by macrophages within 24 h was found for inhaled 20 nm titanium dioxide particles. For comparison, macrophages uptake of 3 to 6 µm particles was two orders of magnitude larger [4]. Contrary to this, microparticles of 1-3 µm in diameter are far better and extensively taken up by AM and those of 1 µm-10 µm diameters are regarded to be the most favourable.

Thus, it seems reasonable sharing the opinion that the microparticles would be more effective than nanoparticles for the pulmonary treatment of intramacrophagic bacteria, especially in terms of breathability. For this reason, new technological approaches have led to the development of hybrid vectors in which nanoparticles are embedded in microparticulate shells so improving the aerodynamic properties of the native nanoparticles and, at the same time, reducing the possible nanoparticle harmful effects [5-7].

References

