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New delivery strategies—needs and prospects

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The ability of the majority of drugs currently in use to diffuse rapidly throughout the body has meant that they can be delivered by a variety of routes with little assistance from delivery systems or devices, other than to maintain stability and ensure uniformity of dose. Two broad categories of agents require additional assistance: large hydrophilic molecules, especially if they are labile or rapidly cleared in their native state, and drugs with a high toxicity. The latter need targeting to specific sites reducing to a minimum the exposure of non-target tissues. This aim is far from achieved in most cases, in spite of the efforts over decades. The former require carrier systems (polymers, particles, dendrimers, vesicles) to ensure protection form hostile enzymes and conditions in vivo, or even to secure absorption also by new routes. These might include uptake through the lymphoid tissue of the gut, nose, bronchus etc, or the tight junctions between epithelial cells or by receptor mediated endocytosis. Carrier particles can provide the locus for the attachment of specific ligands to aid specific interactions with cell surfaces.

There have been proposed many targeting strategies but sober examination of the success, as measured by target tissue/plasma ratios often reveals only modest trends to specific uptake. Some complexes like antibody-drug complexes have been disappointing because their molecular bulk and poor diffusional characteristics have been less than optimal and because, for example, tumour antigens either change in the course of disease progression, or are not expressed on accessible surfaces.

Biopharmaceutics has in the last 30 years taken the subject of pharmaceutics, which was very materials oriented into the area of understanding the interactions of delivery systems with the body, in terms of absorption and distribution. Molecular biopharmaceutics is the development of this trend where interactions between carriers and targets are sought at molecular level. The interaction of drugs has long been considered in this way, but the increased complexity and size of carriers means that new science has to be learned, for example about the cooperativity involved in the interactions between carriers bearing perhaps several hundred specific ligands with multiple cell surface groups. New materials for new carriers are also required to ensure that we can build specific supramolecular structures of defined properties and dimensions to achieve uptake. Nature has evolved many ingenious systems to deliver endogenous molecules to desired sites. We would do well to understand and replicate the super efficiency of neurotransmitter vesicles, for example, in the search for biomimetic systems, or systems which respond to stimuli preferably generated by the pathological tissue being targeted. Nanotechnology and its application to pharmaceutical science will bring rewards in the design of systems and devices. Submicron-scale devices have already been fabricated as reservoir systems; three-dimensional printing technology now allows the production of micro-precision 'tablets'. On another level, there is the need to individualise therapy for a patient population varying in age, ethnicity and pathologies; we must invent a simple patient profile which will be useful to prescribers and pharmacists in the choice of the most appropriate delivery system. Without these macro-developments the micro- and nano-scale progress will be to little avail. The prospects are good, but the challenges great.