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Pharmaceutical Nanotechnology: Past, Present and Future

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The nanotechnology, which is the creation of materials at the nanometer scale, is in fact key area in science and technology which has been extensively explored during the last decades and represents one of the most important directions in the technological developments of the leading countries in the 21st Century. Particularly in the field of drug delivery, the use of pharmaceutical nanocarriers seems to enhance the *in vivo* efficacy of many drugs both in pharmaceutical research and in clinical trials. Despite the efficacy of many drugs used nowadays in clinics, sometimes these exhibit some technological limitations, such as poor solubility or lack of specificity leading to numerous side effects that reduce the quality of life.

Liposomes or phospholipid-based nanovesicles were accidentally discovered in mid-sixties by Alec Bangham. Following their discovery, quickly liposomes started to be studied in order to exploit the capsular and biocompatibility properties of the lipid membrane in drug delivery applications. Thus, liposomes have passed from a scientific curiosity to "magic bullets" to carry drugs and can be considered one of the most popular nanocarriers for delivering many biologically active substances. With the objective to improve physical and/or chemical stability of liposomes or to improve therapeutic efficacy, other types of liposomes were developed, such as niosomes, Transfersomes®, Ethosomes®, Phytosomes®, pegylated liposomes and immunoliposomes. Pegylation of liposomes, i.e. attachment of polyethylene glycol molecules at the surface of the nanocarrier, promotes an increase in circulation time after intravenous administration, potentiating the arrival to the target site of action. Nowadays, there are some marketed formulations based on liposomes and pegylated liposomes.

Following to liposomes, other nanocarriers have been developed such as micelles, polymeric nanoparticles, lipid nanoparticles and dendrimers. Micelles are formed by amphiphilic molecules, self-assembled when these are in the critical micelle concentration. One of the significant disadvantages of micelles is their poor physical stability, since they may dissociate upon dilution. Polymeric nanoparticles are colloidal systems made mainly by biodegradable polymers such as chitosan, alginates, poly-D,L-lactide-co-glycolide (PLGA), polylactic acid, poly-ε-caprolactone, and proteins, such as albumin and gelatins. The major inconvenient associated to polymeric nanoparticles is the use of organic solvents for their production. However, dependently of the production methods and the used drugs and polymers, it is possible to work with less toxic solvents. To overcome this drawback of polymeric nanoparticles, in the beginning the 90's, the lipid nanoparticles were developed, using process free of organic solvents. The first generation of lipid nanoparticles is called Solid Lipid Nanoparticles (SLN) and is composed only by solid lipids, while the second generation is called Nanostructured Lipid Carriers (NLC), composed by solid and liquid lipids. In both cases, the nanoparticles remain solid at room and body temperature. At the beginning of the third millennium, researchers have paid more attention to application of dendrimers as drug delivers. Dendrimers are the hyper branched and uniformly distributed macromolecules, with many arms emanating from a central core, that possess definite molecular weight, size, shape and specific chemical and physical properties including drug entrapment properties.

Considering the research about nanocarriers as drug delivery systems, we can verify that this field of study is at the forefront of the science, with numerous published papers.

Additionally, there are on the market some pharmaceutical preparations based on liposomes, such as Daunoxome®, Doxil®, Marquibo®, AmBisome®, and albumin nanoparticles of paclitaxel, Ambraxe®,and much more are in clinical trials.

These market approval medicines can be viewed as a landmark not just for liposomal or albumin-based drug delivery technology but also for nanomedicine.

The trend of global research is based on the attempt to obtain systems increasingly small, and therefore, nanotechnology overlaps microtechnology. Thus, nanotechnology is a promising area that, in the last years, has shown surprising results.

The near future may hold the emergence of new commercial nanocarrier-based products. However, this technological revolution is a challenge, since the risks are high in terms of investment, but increasing the evidences about the benefits of nanotechnology, the interest by the pharmaceutical industry will also increase.

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