Complexity on the nanoscale and the development of Drug Delivery nano Systems (DDnSs)

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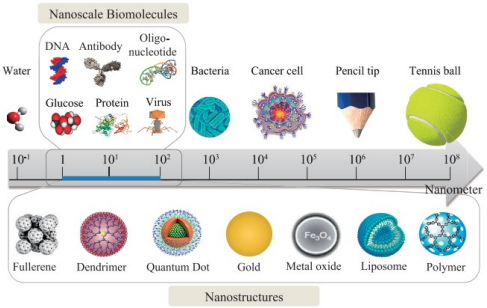
Complex systems are defined as those containing many interdependent constitutes which interact nonlinearly (1). It is of interest to consider the definition of small systems (10^{-6} m to 10^{-9} m) and their thermodynamic profile that affects their effectiveness as drug delivery nanosystems (DDnSs). **'Small system'** is a system which has a size diameter smaller than the range of the interactions of the forces acting on the system itself (2, 3, 4). Small systems differ from those at a macroscopic scale and deviate from classical thermodynamics. **Nanotechnology** in therapeutics is an attractive scientific field that provides innovative medicines and vaccines. More specifically, nanotechnology exhibits a tremendous potential for the diagnosis and treatment of several diseases, thus becoming an indispensable tool in several areas of medicine. It is used for the preparation of nanocarriers, which can improve both the pharmacokinetics and the stability of a drug and can reduce the occurrence of toxic phenomena. Modern therapeutic and prophylactic products are based on the development of innovative nanodevices such as lipid nanoparticles, liquid crystals, dendrimers, polymers, quantum dots etc. (**Fig.1**), that can deliver biomolecules to the injury tissues. The development of DDnSs relates to the level of complexity and to the thermodynamic profile of the nanoscaled drug delivery systems. It is of interest to point out that the internal (short range order) complexity and morphology of artificial nanostructures (i.e., liposomes, lipid nanoparticles, micelles, dendrimers etc.) as innovative carriers of drugs and therapeutic agents or genetic based vaccines, should be evaluated. The integration of Artificial Intelligence (AI) with nanotechnology will facilitate and optimize the development of nanomaterials and nanostructures, affecting several scientific fields and leading to a broad range of applications and smart conventional or nano formulations.

In my intervention, I will discuss examples of applications of complex small nanoscaled drug delivery platforms as nanotherapeutics. The morphological pattern of complex nanoscaled DDnSs is presented using figures taken by cryo-Transmission Electron Microscopy (cryo-TEM) (**Fig 2**) (5). The beauty of drug delivery systems on the nanoscale and their lyotropic properties (i.e., different organization of molecules in the bulk formulation) relate to their morphology. The morphological characteristics of DDnSs follow the order of the natural harmony. The self -assembly process is the driving force to produce new and effective formulations based on the complexity that drives the adaptation, the evolution, and the effectiveness of innovative DDnSs carrying biomolecules for therapeutical purposes.



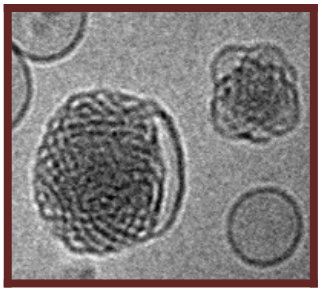


Fig. 1. Comparison of different nanoscale biomolecules and nanoparticles;, **Fig.2**. Complex Artificial bio-nanostructures (cryo-TEM)

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