Peptides and Therapeutics

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Recent years have witnessed a revival in the field of peptides. In addition to being important biochemical tools, peptides are involved in therapeutic areas as diverse as cancer, antimicrobials, antivirals, central nervous system, analgesia, asthma, allergy and Ca^{2+} metabolism, among others. Today, more than 40 peptides are currently on the market, 4 more are in registration, 200 are in clinical phases and more than 400 are in advanced preclinical trials. The latest breakthrough in the use of peptides as pharmaceutical agents is T-20 (Fuzeon, Enfuvirtide), a peptide of 36 amino acids that docks on the surface of the AIDS virus, thereby preventing the virus from entering human blood cells. Furthermore, peptides show potential not only in drug delivery systems but also as vaccines, by enhancing cellular uptake and drug targeting.

Success in the field of peptide research is partly attributable to the fact that it is now possible to synthesize almost any peptide on both small and large scales. In this regard, the solid-phase methodology proposed by Merrifield in the late sixties and fine-tuned over time has been crucial. Thus, solid-phase strategies together with *combinatorial* chemistry have fuelled the introduction of peptides in the above-mentioned therapeutic areas.

In this communication, and taking advantage of our extensive experience in the field, several topics will be discussed. First of all, we present an overview of the use of peptides in medicine, in particular as anti-tumoral agents. Next, the most used synthetic strategies, which involve solid-phase, a combination of solid-phase solution, and chemical ligation, will be discussed. Finally, the use of foldamers (non-natural peptides that exhibit structure) and peptide-based dendrimers for cellular uptake will be reviewed. These unnatural oligomers offer a number of advantages over other well-known drug delivery systems.