At the present time, an important proportion of the effort made by research groups for the development of new forms of drug administration is centered in the use of nanotechnology. The «nano-systems» (nanospheres, nano-capsules, liposomes, etc.) exhibit great advantages for their therapeutic use in comparison with traditional systems of administration. Said advantages include the protection of drugs against the external atmosphere (pH, enzymes, etc.) and high interaction with tissues and biological fluids thanks to high specific surfaces. All these characteristics have helped the “nano-systems” become the best vehicle for the administration of active substances coming from biotechnology, such as peptides, proteins and nucleic acids. Specifically, in ophthalmology, both nanoparticles and liposomes have demonstrated to be useful for increasing the bio-availability of a broad range of active molecules (1).

Dendritic polymers comprise a new generation of «nano-systems» that have stirred up a great interest in recent years, among other things due to their high potential as forming agents of drug vehicles. From a chemical point of view, the dendrimers are synthetic polymeric macro-molecules of different nature (peptide, lipidic, polysaccharide, etc.). A typical dendrimere is formed by a central molecule with several «branches», which in turn branch out originating a three-dimensional globular structure of concentric layers. Each stage of the chemical synthesis is perfectly controlled, giving rise to an organized structure of a specific size which exhibits on its surface a defined number of functional groups. The presence of those functional groups (amino, carboxyl, hydroxyl, etc.) on the surface of the dendrimers confer to these agents a major part of their usefulness in therapeutic applications (2).

The functional groups mentioned above provide the dendrimers with a determined charge at the physiological pH (anionic or cationic). In particular, the cationic dendrimers are of interest for their application in the ocular topical pathway since they exhibit high interaction with the mucins of the corneal epithelium which are loaded negatively in physiological conditions by the presence of sialic groups. This electrostatic interaction converts these dendrimers in mucoadhesive compounds able to generate an increase in the contact period of the pharmaceutical form (and the drug that it contains) on the surface of the eye. In addition, the cationic nature of these dendrimers also induces electrostatic interaction with proteins of the epithelial intercellular unions, generating a temporary reorganization of these structures and an increase of their paracellular permeability (3,4). These properties are attractive for the use of these polymers as promotional agents of the penetration of active substances through the cornea.

In what concerns the encapsulation of the drug, the hydrophobic active molecules can encapsulate inside the dendrimere, thus increasing their water solubility (5). On the contrary, the hydrophilic molecules can be united to the surface of the dendrimere due to their superficial characteristics or by covalent unions, hydrogen bridges, electrostatic interactions, etc. In this sense, the cationic dendrimers feature the enormous advantage of being able to encapsulate oligonucleotides (of polyanionic
nature), which in addition makes them exceptional candidates for the development to formulations in genic therapy (6).

All the characteristics mentioned above have led to a substantial increase of the study of dendrimeres in recent for administration of drugs. Nevertheless, while in other pathways such as the oral, intravenous or transdermal pathways, studies are more advanced, for instance in cancer therapy against in experimentation animals (7), a small number of papers are published for the ophthalmic pathway. Even so, the results obtained are highly promising, as in the case of the topical coadministration of pilocarpine and tropicarpine with polyamidoamine dendrimeres (PAMAM), a study in which a maintained and lasting pharmacological effect in experimentation animals was observed, in contrast with conventional treatment (drug in solution). In addition, the formulation developed with dendrimeres exhibited better tolerance than that obtained for other linear cationic polymers (8).

Other authors have also begun to explore the use of dendrimeres for genic therapy in ophthalmology. The first studies have focused on fighting neovascularization in patients with diabetic retinopathy or age-related macular degeneration. In these cases, the intraocular administration of associated lipidic dendrimeres to oligonucleotides with the capacity of reducing the transcription of the vascular endothelial growth factor (VEGF), one of the main associated angiogenic factors of neovascularization, provided protection against neovascularization in experimentation animals for over one month (9).

It is obvious that the interesting results obtained in the ophthalmic pathway allow for a promising future for the development of ophthalmic formulations based on dendrimeres, not only as nonviral vehicles for genic therapy, but also to improve the bioavailability of other therapeutic agents.

REFERENCES