Superparamagnetic iron oxideeloaded lipid nanocarriers incorporated in thermosensitive in situ gel for magnetic brain targeting of clonazepam

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The objective of the study was to target clonazepam to the brain through the intranasal olfactory mucosa using nanolipid carriers loaded with superparamagnetic iron oxide nanoparticles (SPIONs) to allow nanocarrier guidance and retention with an external magnetic field. For improved delivery, the nanolipid carriers were incorporated in a thermosensitive mucoadhesive in situ gel. Different nanolipid carriers including solid lipid nanoparticles and nanostructured lipid carriers (NLC) were prepared and characterized with respect to particle size, zeta potential, entrapment efficiency, and in vitro release. The NLC composed of 3 solid lipids (Compritol® 888, stearic acid, and glyceryl monostearate) and 2 liquid oils (oleic acid and glyceryl monooleate) showed the most satisfactory characteristics and was loaded with SPION (NLC/SPION). Both formulae (NLC and NLC/SPION) were incorporated in an optimized thermosensitive mucoadhesive in situ system composed of 15% pluronic 127 and 0.75% sodium alginate and evaluated for the anticonvulsant action in chemically induced convulsive Swiss Albino mice. The treatment of animals with NLC/SPION significantly prolonged the onset times for convulsion and considerably protected the animals from death. One can thus hope for the emergence of a new intranasal treatment of epilepsy with consequent decrease in peripheral side effects of clonazepam.