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### **In vitro quantitative comparison study of insulin SLNs and PLGA NPs as potential carriers for the brain delivery of intranasal insulin**

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The brain disorders complexity, and high costs of drug development process stand behind the absence of satisfying anti-neurodegenerative therapies. Brain-targeting intranasally-applied nanoparticles represent an optimal way to deliver these therapies as it guarantees the direct transport of the APIs to the brain (N2B). The brain insulin dysfunction has pertained to cognitive processes as insulin constitutes a neuroendocrine link between metabolism and cognition. Solid-lipid nanoparticles (SLNs) and polylactic-co-glycolic acid nanoparticles (PLGA NPs) represent two possible candidates for the N2B of insulin. Four types of Nanoparticles SLNs, PLGA NPs, chitosan-coated SLNs, and PLGA NPs were formulated, then, an in-vitro comparison to the native insulin took place. The physicochemical assessments demonstrated insulin stability in the nanoparticles. The in-vitro experiments showed the superiority of SLNs regarding the dissolution, mucoadhesion, and permeation behaviors over PLGA NPs with a further enhancement by the chitosan-coating. The in-vitro cell line investigations revealed the nanoparticles' safety for the intranasal application and confirmed the in-vitro experiments regarding the nasal mucosa permeation, but not the BBB permeation, because the native insulin is transported actively. In conclusion, an optimal N2B insulin formulation should combine native insulin and insulin-SLNs as the former obtains the immediate effect while the latter ensures effective brain pharmacokinetics.

#### References

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