**Application of Quality by Design Approach in Nanoparticle Formulation Development**

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**Background and aims.** Quality by Design (QbD) is a systematic approach to pharmaceutical development that enhances product quality through understanding formulation and process parameters. With nanotechnology advancement in drug delivery, ensuring consistent quality and scalability of nanoparticle formulations remains challenging. This study applied QbD principles to optimize three distinct nanoparticle systems for improved drug delivery.

**Methods.** QbD methodology was applied to nanostructured lipid carriers (NLC) loaded with amyrin-rich extract and lycopene, self-assembled chitosan-phospholipid nanoparticles containing luteolin, and cubosomes loaded with mangiferin. Quality Target Product Profile (QTPP) targeted particle size <200 nm, polydispersity index <0.3, maximum entrapment efficiency, and stable zeta potential. Critical Quality Attributes (CQAs) and Critical Process Parameters (CPPs) were identified through literature analysis and risk assessment matrices. Design space optimization used experimental design approaches.

**Results.** Risk analysis showed particle size, entrapment efficiency, zeta potential, and PDI represented >80% of quality assessments across all systems. For NLC, surfactant and lipid concentrations were most critical. Self-assembled nanoparticles showed high sensitivity to lecithin-chitosan ratio and API concentration. Cubosome formulations were primarily influenced by mangiferin concentration and GMO:P407 ratio. All optimized formulations achieved target specifications (Table 1).

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| **Nanoparticle System** | **Size (nm)** | **PDI** | **Zeta Potential (mV)** | **EE (%)** |
| **Amyrin-NLC** | 178.6 ± 3.7 | 0.216 | -57.7 ± 0.4 | 100 |
| **Lycopene-NLC** | 155.8 ± 5.2 | 0.207 | 46.17 ± 3.45 | 100 |
| **Luteolin-SA** | 143.1 ± 2.2 | 0.202 | -17.50 ± 1.70 | 90.39 |
| **Mangiferin-Cubosome** | 156.03 ± 0.5 | 0.186 | 57.58 ± 1.38 | 84.41 |

**Table 1.** Optimized nanoparticle formulations meeting QbD target specifications.

**Conclusion/Discussion.** QbD principles successfully optimized diverse nanoparticle formulations, providing robust design spaces for consistent manufacturing. This approach offers valuable guidelines for future nanoparticle development and supports scale-up processes while maintaining product quality and regulatory compliance.

**References:** (1) Li J, Qiao Y, Wu Z. J Control Release. 2017;256:9-18. (2) Bastogne T. Nanomedicine. 2017;13:2151-2157.