

PL-14

Advanced Drug Delivery Systems: From Nano- and Microparticles to Smart Pills

ISTVÁN ANTAL

*Department of Pharmaceutics, Semmelweis University, Hógyes Endre St. 7, H-1092, Budapest, Hungary**Correspondence: antal.istvan@pharma.semmelweis-univ.hu***Keywords:** *Multiparticulate drug delivery systems, microparticles, microspheres, microcapsules, microfluidics*

1. Introduction

Nowadays, there is a growing interest toward the development of advanced drug delivery systems that provide new opportunities for improving the safety and efficacy of drug therapy. The multiparticulate structured formulation using advanced excipients may serve as a drug delivery system capable of increasing efficacy and / or reducing side effects through innovative technological solutions. The active ingredient is an essential component of pharmaceutical formulations, but the dosage form is the one which carries and liberates its contents as drug substance targeted to the site of action. In case of multiunit systems, the dose is distributed in many small separate particles, which carry and release a part of the dose, hence the malfunction of an individual subunit does not cause the failure of the whole dosage form (1).

Multiparticulate drug delivery systems offer several advantages both to patients and developers:

- choice of dosage form for the desired route (peroral tablets, parenteral injections),
- modified and targeted (even site-specific) drug delivery,
- more expectable pharmacokinetics with decreased intra- or inter-subject variability,
- more homogenous distribution,
- stable fixed-dose combinations of drugs
- dose titration and less dose-dumping,
- patient centricity through better compliance and adherence ,
- individual therapy,
- better stability,
- better compatibility through isolation,
- innovative products with a prolonged life cycle,

The pharmaceutical formulation is expected to provide optimized pharmacokinetics with appropriate plasma level, onset and duration of action.

Patient centricity is also challenging for specific groups (e.g., elderly or children), and for some conditions (e.g., swallowing difficulty, mental or physical illness). Innovative drug technology and drug delivery systems allow the desired pharmacokinetic profile, adequate bioavailability, and more favorable dosing regimens.

Recently, many novel formulations containing multiparticulate systems have gained therapeutic and diagnostic significance. Microparticles, microspheres, and microcapsules are common components of multiparticulate drug carriers that, by virtue of their structural and functional capabilities, offer numerous therapeutic benefits for patient-centered drug application. Depending on the mode of application, they may be incorporated into solid (capsules, tablets, sachets), semi-solid (gels, creams, pastes) or liquid (solutions, suspensions, or parenteral) dosage forms (2).

Microparticles' size ranges 1-1000 μm and can be characterized as matrix systems in which the drug is homogeneously dispersed, either dissolved or homogeneously suspended (*Figure 1*). Traditional microsphere structure contains solid or liquid drug substance dispersed or dissolved in a matrix. Microcapsules are reservoirs of microscopic size surrounded by a wall, that is able to modulate the release from the reservoir.

Nanoparticles (e.g., nanocrystals, vesicles, conjugates) are useful not only for solubilization but also for reducing side effects through targeted drug delivery. The microparticles increase applicability and, as independent drug delivery units, result in predictable and predictable blood levels. The structural and morphological (size) properties of the nano- and microparticles can be controlled by their release, and their properties can be "smart triggering". Reconstitution provides a good opportunity to preserve the structure during storage. New methods have been developed for conven-

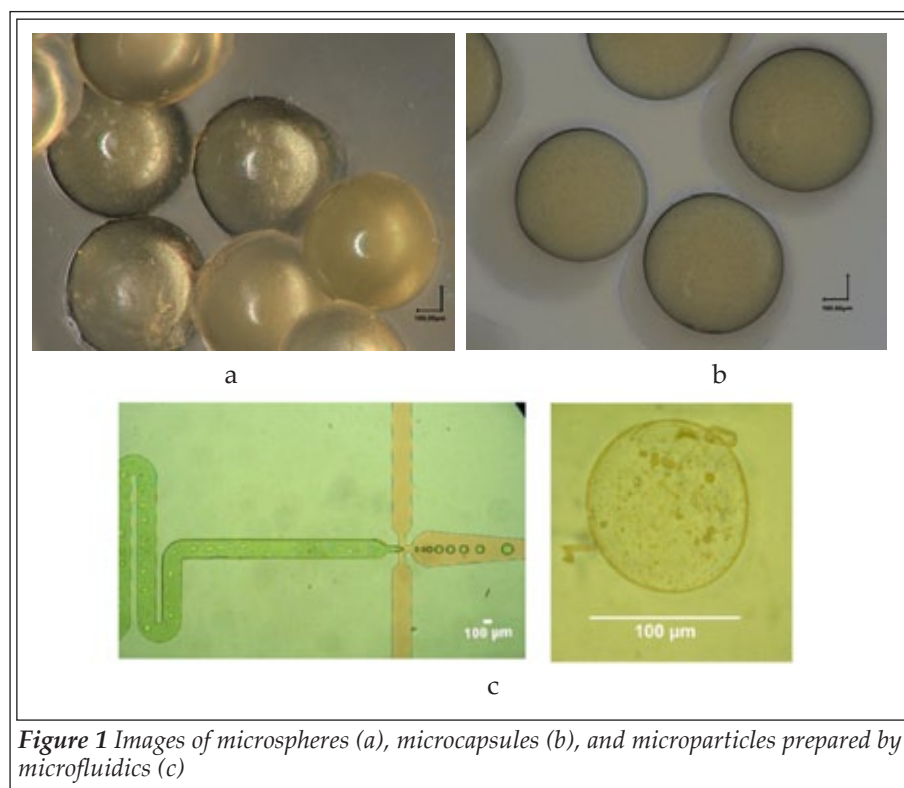


Figure 1 Images of microspheres (a), microcapsules (b), and microparticles prepared by microfluidics (c)

Digital pharmaceutical technology represents a new development trend, combining formulation and information technology solutions for tracking as well as to enable treatment management, collaboration and therapeutic adherence.

2. Conclusions

Nano and microparticles alone or combined with smart triggering mechanisms offer a wide range of possibilities for the improvement of therapeutical effectiveness and tolerability, as well as patient centricity with increased compliance and adherence. Large number of polymeric excipients and manufacturing processes can be used for

tional coacervation (e.g. freeze-drying, spray-drying, microfluidic flow focusing, etc.), and various structures provide opportunities for fine-tuning the release mechanisms and optimizing the pharmacokinetic profile.

The process of drug release of microparticulates-produced by special manufacturing technologies and/or possibly containing special excipient(s) – is the result of various phenomena, mechanisms (dissolution/diffusion, osmotically driven release, erosion).

Beside classical coacervation, fluid and spray processing, embedding also microfluidics shows promising results in microparticle production.

In the case of smart drug delivery microparticle systems, the release of the drug occurs by a triggering mechanism which can be internal or external and be classified as physical, chemical, or even microbiological.

formulations and their structures allow to modulate drug release mechanisms and to optimize the pharmacokinetic profiles. By now, it has become clear that the right dosage form is an important prerequisite for the success of therapy, and that patient-centered drug treatment requires a paradigm shift in the field of pharmaceutical technology.

3. Acknowledgments

The author is grateful to all coworkers in the field of research and development.

References

1. Lengyel, M., Kállai-Szabó N., Antal V., Laki A.J., Antal I.: *Microparticles, Microspheres, and Microcapsules for Advanced Drug Delivery*, *Sci. Pharm.*, 3: 87 (2019).
2. Lengyel, M., Balogh E., Szerőczei D., Dobó-Nagy Cs., Pápay Zs., Antal, I.: *Study on process parameters and optimization of microencapsulation based on phase separation*, *Eur. J. Pharm. Sci.*, 25: 273-278 (2018).