

## Summary of stage I / 2025

The project proposes the development of an original, combined topical formulation with dual therapeutic action by incorporating the synthetic active substances Nimesulide (anti-inflammatory agent) and Chlorhexidine (anti-infective agent), as well as the natural active compound *Boswellia serrata* extract, into bilosome-type nanovesicles as the carrier matrix. The final goal is to improve the release of the active substances, increase their bioavailability, and optimize their biopharmaceutical properties in order to achieve an efficient and long-lasting therapeutic effect.

Bilosomes (BIs) represent a new generation of lipid nanovesicles enriched with bile salts, having superior penetration capacity through biological membranes. Their structure consists of three main components: *i*) phospholipids (lecithin, cholesterol, phosphatidylcholine, etc.), *ii*) nonionic surfactants (synthetic polyoxyethylene-type compounds such as Tween or polysorbate–Span), and *iii*) bile salts (sodium deoxycholate, sodium taurocholate, sodium glycocholate), which serve to improve skin permeability. Bilosomes with these properties are thus capable of delivering active components to the deep layers of the skin when administering various hydrophobic or hydrophilic pharmaceutical active substances transdermally.

The results obtained in Stage 1 within the five planned activities (A1.1–A1.5) are as follows:

1. Within activity **A1.1** (Preparation and optimization of bilosome production parameters – part 1), the experimental design for obtaining the bilosomes was developed using dedicated software, Design Expert. Based on the generated experimental design, bilosomes containing soy lecithin, Span 80, and sodium deoxycholate in various proportions were synthesized using the thin-film hydration method.
2. Activity **A1.2** (Characterization of bilosomes – part 1) focused on characterizing the obtained bilosomes through dynamic light scattering (DLS) to determine particle size and transmission electron microscopy (TEM) to elucidate their morphology.
3. Activity **A1.3** (Planning, coordination, monitoring, and evaluation of research activities – part 1) involved preparing the work plan and synchronizing activities A1.1 and A1.2. Additionally, the project's webpage was created: <http://www.itim-cj.ro/bilateral/dual-nano/>
4. The results of activity **A1.4** (Financial coordination of project implementation – part 1) consisted of ensuring on-time logistics and supplies necessary for carrying out activities A1.1 and A1.2.
5. Activity **A1.5** (Planning and organizing travel of team P members to the CO institution – part 1) in this stage consisted of organizing online meetings between the two research teams, the team from INCDTIM and the team from USMF Nicolae Testemițanu in the Republic of Moldova.