novel process for the impregnation of suture threads with thermally sensitive chemicals

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The use of supercritical CO_2 ($scCO_2$) in the treatment of medical and pharmaceutical materials has attracted a growing interest. Beside the well-established processes such as extraction of active compounds and impurities removal, impregnation processes of material with active pharmaceutical ingredients (APIs) are becoming nowadays very important. Classical impregnation methods based on solvents such as hydrocarbons, ethanol or water show several drawbacks such as low diffusion rate, long contact time and high process temperatures. Moreover, in many cases hazardous solvents are used even if these imply increased efforts to remove the solvent or additional installation costs. There are several advantages in the use of $scCO_2$ as impregnation solvent such as high diffusivity, low viscosity and its peculiar tuning of solvation properties based on temperature and pressure. Furthermore, the mild temperatures needed to achieve supercritical conditions allows one to treat both temperature sensitive materials and load thermally sensitive chemicals without damaging them. These characteristics, together with the low toxicity and the negligible residual left after the process, make $scCO_2$ a very interesting impregnation solvent for medical products such as suture threads or implantable membranes. However, a $scCO_2$-based process is still challenging, since the impregnation process must assure homogeneous conditions through the entire batch volume, in order to achieve a homogeneous API dispersion in the device and a robust reproducibility.
The aim of this work is the development of a process, for the loading of thermally sensitive APIs, able to face these challenges, and thus leading to a product with homogeneous drug dispersion and reproducible characteristics. As a proof for the industrial process, ketoprofen, a nonsteroidal anti-inflammatory drug, was loaded on a suture threads with a length of several meter. The innovative nature of the process lies in the horizontally placed process chamber equipped with a special rotatable basket. The basket, specially designed to increase the contact area between suture thread and $scCO_2$, leads to a uniform exposure of the thread with $scCO_2$, while its rotation ensures homogeneous conditions throughout the entire batch volume, enhancing the mass-transfer and thus the impregnation of the drug inside the suture thread. Moreover, the absence of surface tension of the $scCO_2$ improves the penetration inside the thread matrix, lowering the glass transition temperature and enhancing the diffusion of ketoprofen inside the thread. These process features turn out to be essential for a homogeneous API dispersion in the suture thread, which is of paramount importance to achieve the desired performances, in terms of drug release rate and thus therapeutic effect. The impregnation experiments were carried at temperature between 35°C and 40°C and at 250 bar followed by a slow depressurization step. The desired concentration inside the suture thread was achieved by fine tuning temperature and pressure in order to solubilize in the $scCO_2$ a sufficient amount of the ketoprofen. The amount of the ketoprofen impregnated as well as the degree of dispersion inside the suture thread were determined by release kinetic experiments whereas mechanical tests were performed to test the integrity of the thread.
The new proposed impregnation process based on the horizontally placed process chamber coupled with the special rotatable basket has proved to be a very promising substitute for classical solvent-based impregnation methods. The tunability of the solvation property of the $scCO_{2,}$ coupled with the special basket design, ensure homogeneous conditions throughout the entire process chamber volume leading to a homogeneous distribution of the ketoprofen throughout the entire suture thread length. Furthermore, due to the homogeneous distribution and the batch to batch reproducibility the proposed process complies with cGMP standards.