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Quality-by-Design (QbD) process evaluation for phytopharmaceuticals on the example of 10-deacetylbaccatin III from yew

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The focus of pharmaceutical product development lies on assuring excellent product quality at the end of a cost-efficient process. The Quality-by-Design (QbD) concept shifts the focus from quality assurance through testing to quality control by process understanding, resulting in very robust processes with high quality product[FDA 2006, ICH 2009, 2009]. QbD was originally intended by authorities for biologics, where product quality proven completely by analytics is not desired. Product quality has to be controlled by means of appropriate processes and operations as well.

These demands were developed in order to improve patients' safety by optimal drug quality at more efficient manufacturing processes reducing costs for healthcare systems. Furthermore, production of biologics includes feedstock variability and complex multi-step manufacturing processes in batch operation with variable lots – condition, which apply to botanicals as well. The use of rigorous (physico-chemical) process modeling in combination with QbD results in a high degree of process understanding. This offers, contrary to popular prejudices, great benefit for manufacturers with little extra effort during development[Kaßing 2012]. The methodical QbD-based approach is pursued to develop a process for extraction and purification of 10-deacetylbaccatin III from yew needles. A short history and key elements of the QbD-based application are introduced.

The line of argument for basic process conception is described and initial risk assessment is shown. Typical raw material variation and vaporization are identified as causes of process variability, therefore, the implications to subsequent process steps are pointed out. Finally, influences of load and flow rate on the chromatographic separation of 10-deacetylbaccatin III are shown to exemplify sensitivity of purification design[Uhlenbrock et al. 2017].

Literature

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