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Book review

Handbook of Isolation and Characterization of Impurities in Pharmaceuticals, Satinder Ahuja, Karen Mills Alsante (Eds.), in: Satinder Ahuja (Ser. Ed.). Separation Science and Technology, Vol. V. Academic Press, San Diego, London (2003). p. 430, ISBN: 0-12-044982-X

The fifth volume in the series Separation Science and Technology, edited by S. Ahuja and K.M. Alsante, contains 14 chapters, which deal with analyses, isolation and characterization of impurities in pharmaceuticals. The outlay is logical and leads readers from regulatory requirements through sample preparation techniques to isolation methods such as thin-layer chromatography (TLC) and column chromatography to characterization employing techniques such as mass spectral (MS) and nuclear magnetic resonance (NMR) as well as hyphenated methods.

As in preceding volumes of the series, the leading specialists in the field provide in-depth review chapters.

An overview of issues concerning the impurities in pharmaceutical materials is presented in the Chapter 1, starting with a definition of what may be considered an impurity. Regulatory guidelines (FDA/USP/ICH) on impurities are briefly explained in the second chapter. Modern methods for detecting and quantifying polymorphic and solvatomorphic impurities in bulk solid active pharmaceutical ingredients are described in the third chapter, such as X-ray diffraction, thermal methods of analysis (TGA and DSC), vibrational spectroscopy (IR, NIR and Raman) and solid-state NMR.

Drug substance, excipients, packaging – and various additives to all these – may be sources of impurities in drug product. Impurities may influence performance and/or stability of drug product due to their chemical reactivity, or ability to introduce a physical change to the dosage form. Systematic overview of sources of the impurities in drug products is presented in Chapter 4.

A brief explanation of how to choose a strategy for investigation and control of both process-related and degradation impurities is offered in Chapter 5. HPLC with UV detection is a widely employed analytical technique for determining degradation impurities during stress-testing. A short overview of problems that may arise while using this technique is provided.

Chapter 6 offers a definitive review of what is a reference standard in pharmaceutical industry. Examples on how to calculate purity and assay of a standard are included.

Chapters 1–6 describe what is considered an impurity in pharmaceuticals and help to clarify the "why" question – i.e. why the industry has to deal with them. Chapters 7–14 provide a detailed overview of "how" to solve a multitude of impurities related problems that are encountered by analytical chemists in pharmaceutical industry.

Specificity is a regulatory requirement for analytical methods that determine the purity of active pharmaceutical ingredients. Therefore, in order to effectively develop methods that would resolve impurities, degradants and matrix components a Key Predictive Sample Set (KPSS) should be defined. The logic behind sample selection for inclusion in KPSS during analytical method development is detailed in Chapter 7. Use of phase-solubility analysis for enhancing tracking of low-level impurities is suggested.

Chapter 8 is devoted to review of sample preparation methods. Both theoretical and practical considerations of the Solid-Phase Extraction (SPE), Liquid-Liquid Extraction (LLE), Supercritical Fluid Extraction (SFE) and Accelerated Solvent Extraction (ASE) methods are briefly covered. Membrane filtration and centrifugation are discussed.

Methods for isolation of impurities are described in Chapter 9 (Thin-Layer Chromatography – TLC) and Chapter 10 (column chromatography). The chapter on TLC is well illustrated (with a minor mishap of HPLC chromatogram missing in Fig. 19 of the chapter). It presents important but sometimes overlooked points on validation of TLC methods for both drug substance and drug product (e.g. effect of prewashing the plate, of chamber saturation, post-development drying time, etc.). Use of TLC and HPLC techniques in tandem in order to isolate and characterize impurities is discussed. Once the impurity profile of the sample is determined it may be necessary to isolate an impurity in relatively significant amounts, for example for structure determination, toxicity studies, etc. The power of column chromatography is needed in most cases in order to overcome problems encountered with conventional separation techniques. Chapter 10 provides an introduction to packing materials and equipment that may be employed for isolating impurities, as well as an outline of how to develop a preparative method.

Mass spectral (MS) characterization of impurities is a topic of Chapter 11. Principles and techniques of impurities characterization are broadly covered, logically leading to strengths of MS analysis, thus allowing the reader to gain

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a better understanding about how a wealth of data obtained could be translated into a successful identification or a structure. The chapter is filled with numerous references (more than 180) that provide for ample further reading.

Chapter 12 describes implementation of NMR in liquid samples for characterization of impurities – from sample preparation to choosing an instrument to results interpretation. Coupling of liquid chromatography to NMR (LC-NMR) is concisely covered. Some hyphenated characterization techniques as chosen by the author are discussed in Chapter 13. Combination of chromatography with Fourier Transform Infrared Spectroscopy (FTIR), MS and NMR spectroscopy is briefly described. Finally, Chapter 14 presents actual case studies detailing designed approach to the process of isolation and identification of impurities. The flowcharts succinctly demonstrate the decision tree of such a process. Real life examples provide for a synthesis of all the information contained in previous chapters and read like the detective stories they are.

I have found this volume to be of value both as a comprehensive guidebook as well as a reference, providing a depth of information and practical advice. There is a wealth of well-illustrated examples and case studies. Most of the references are from the 1990s up to 2001 affording for further reading. This book should be of high value to all scientists working in pharmaceutical industry.

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