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Analytical procedures for the quality control of pharmaceuticals in terms of residual solvents content – challenges and recent developments

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Highlights

- residual solvents in pharmaceuticals – problems and challenges
- overview of regulatory and general methods
- sample preparation techniques for analysis
- final determination methods
- recent developments in the determination of residual solvents

Abstract

Residual solvents play an important role in the synthesis of drug substances and in product formulations. At the same time they pose a problem and must be removed, because many of them have toxic or environmentally hazardous properties. Therefore, constant monitoring of quality control is needed. In this paper, we present an overview of regulatory and general methods described by various Pharmacopoeias. Next, the most commonly used methodologies for the determination of residual solvents in different pharmaceutical samples are reviewed to demonstrate their limitations, which form the basis for discussion about new methods. Several interesting new alternatives for sample preparation and gas chromatography (GC) separation are presented using examples from recent literature. The techniques described are direct injection, headspace analysis with different modifications and variations, liquid extraction, single-drop microextraction, solid-phase microextraction. Various GC