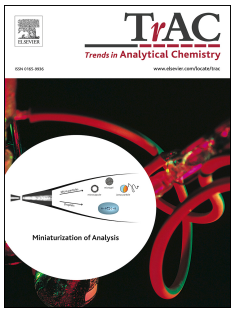
Accepted Manuscript



Critical review of reports on impurity and degradation product profiling in the last decade

Sándor Görög

PII: S0165-9936(17)30323-0

DOI: 10.1016/j.trac.2017.09.012

Reference: TRAC 15004

To appear in: *Trends in Analytical Chemistry*

Received Date: 22 August 2017

Revised Date: 1 September 2017

Accepted Date: 5 September 2017

Please cite this article as: S. Görög, Critical review of reports on impurity and degradation product profiling in the last decade, *Trends in Analytical Chemistry* (2017), doi: 10.1016/j.trac.2017.09.012.

Critical review of reports on impurity and degradation product profiling in the last decade

Sándor Görög

Chemical Works Gedeon Richter Plc., Budapest, Hungary

E-mail: gor4745@t-online.hu

Drug impurity and degradation profiling mean the detection, structure elucidation and quantitative determination of impurities and degradation products in bulk drug materials and pharmaceutical formulations. This is today one of the most important fields of activities in pharmaceutical analysis. The reason for this is that unidentified, potentially toxic impurities are health hazards, and in order to increase the safety of drug therapy, impurities should be identified and determined by selective methods.

The aim of this review is to characterise the state-of-art in the field of impurity and degradation profiling of drugs based on papers published in the last decade. The separation and determination of impurities and degradants with a known structure are discussed, but emphasis is placed on the structure elucidation and determination of new (unknown) impurities and degradation products by off-line and on-line chromatographic – spectroscopic methods. The analytical aspects of enantiomeric purity of chiral drugs are also discussed.

Keywords: Impurity; Degradant; Chromatography; Spectroscopy; Hyphenated methods; Enantiomer

1. Introduction

The “International Council for Harmonisation and Technical Requirements for Pharmaceuticals for Human use (ICH)” presents the following definitions for impurities and impurity profile in new drug substances [1]. An impurity is “Any component of the new drug substance that is not the chemical entity defined as the new drug substance.” An impurity profile is “A description of the identified and unidentified impurities present in a new drug substance”. Impurity profiling is the common name of analytical activities for the detection, identification/structure elucidation and quantitative determination of organic and inorganic impurities as well as residual solvents in bulk drugs and pharmaceutical formulations [2].

The aim of this review paper is to give an overview on the state-of-art in impurity and degradation profiling of drugs based on papers published in the last decade. References to earlier publications on this topic can be found in the author’s book [2] and in the author’s review paper [3] (citing papers published up until 2000 and between 2000 and 2007, respectively). Only papers dealing with the identification and quantification of related organic impurities and degradation products are reviewed here: inorganic impurities are outside the scope of this paper. The