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Review

Residue analysis: Future trends from a historical perspective

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ABSTRACT

A residue is a trace ($\mu g\,kg^{-1}$, $ng\,kg^{-1}$) of a substance, present in a matrix. Residue analysis is a relatively young discipline and a very broad area, including banned (A) substances as well as registered veterinary medicinal products (B substances). The objective of this manuscript is to review future trends in the analysis of residues of veterinary drugs in meat producing animals out of historical perspectives. The analysis of residues in meat producing animals has known a tremendous evolution during the past 35–40 years. In the future, it can be foreseen that this evolution will proceed in the direction of the use of more and more sophisticated and expensive machines. These apparatus, and the necessary human resources for their use, will only be affordable for laboratories with sufficient financial resources and having guarantee for a sufficient throughput of samples.

Contents

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1. Introduction

Historically seen, the analysis of residues of chemicals in foods of animal origin is a relatively young discipline. In the BENELUX (Belgium, The Netherlands and Luxemburg) one can say that residue analysis started in the late 1960s or the early 1970s. The BENELUX SP/Lab/h documents illustrate the cooperation in residue analysis between several laboratories in The Netherlands and Belgium: the first traceable document dates from 1978 [1]. In most European countries research on residues and the application in regulatory control on slaughter animals started later. A residue may be defined as a trace of a substance, present in a matrix (e.g. meat, urine, etc.) after some kind of administration (e.g. within the framework of veterinary practice or illegal use) to an animal. In all cases, concentration levels in the ppb concentration range ($\mu g\,kg^{-1}$) or even lower (ppt; $ng\,kg^{-1}$) have to be detected. The substances involved may be divided into two major classes according to council directive 96/23/EC [2]: group A and B substances. Group A involves the growth promoters abused in animal fattening and the "no maximum residue limit (MRL)" substances and may be subdivided into four major groups: anabolics or anabolic steroids, thyreostats, beta-agonists or repartitioning agents and Annex IV substances. Corticosteroids (CoST) may also be abused as growth promoters, although they belong to the class of veterinary drugs. In this article CoST are treated as A substances. Group B contains the veterinary drugs or veterinary medicinal products (VMPs): antibacterial substances, other VMPs as anthelmintics, coccidiostats, carbamates and pyrethroids, sedatives, non-steroidal anti-inflammatory drugs (NSAIDs) and other pharmacologically active substances. The analytical requirements for both groups are different.

For banned (A) substances the emphasis lays on the identification of the substances in a large number of matrices (e.g. meat, urine, hair) in a concentration as low as possible (zero tolerance principle). In this case, at first qualitative multi-residue methods have to be developed and secondly quantificative methods. Recent developments in the use and abuse of growth promoters are reviewed [3]. For B substances having a MRL, methods for the quantitative determination of the substances in edible matrices only (e.g. meat, liver) have to be worked out. In most cases the MRLs of B substances are a magnitude 10–100 times higher than the recommended concentrations (minimum required performance levels; MRPLs) of the A substances [4]. A recent review on the analytical strategies for residue analysis of veterinary drugs and growth-promoting agents in food-producing animals was published in this journal [5].

In the early 70s thin layer chromatography (TLC) was the method of choice for the qualitative detection of banned substances (thyreostats and certain anabolics at that time). The reasons therefore were the specificity, the simplicity of development in two dimensions and the possibility of reaching low limits of detection for an acceptable budget (often using fluorescence detection). The only alternative with acceptable limits of detection – at that moment – was gas chromatography with electron capture detection (GC-ECD). High-performance liquid chromatography (HPLC) with UV detection was introduced in the middle 70s, but the first instruments were expensive and not robust. UV detection does also not match the specificity and limits of detection needed for A substances. Fluorescence detectors were only introduced later. However, for the quantitative determination of B substances UV detection and post-column derivatisation was often used. During the 90s more and more affordable gas chromatography–mass spectrometry (GC–MS) apparatus appeared on the market and the transition from TLC (and HPLC) to GC–MS methods was ongoing. Somewhat later on (end of the 90s), LC–MS^n belonged more and more to the mandatory standard equipment of a residue laboratory. In Fig. 1 the evolution of methods used in residue analysis in function of time is presented.

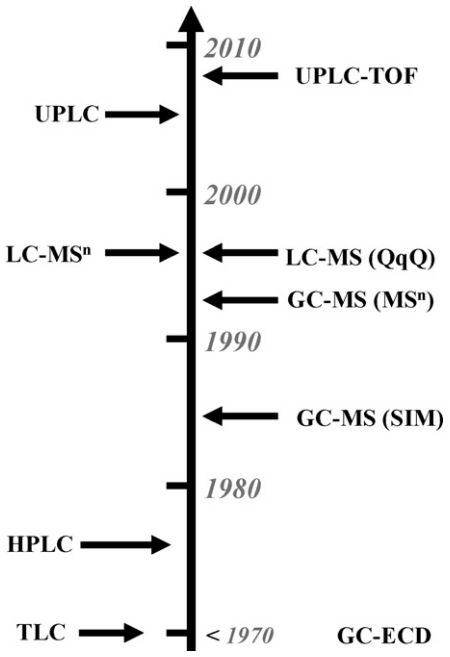

Fig. 1. Evolution of methods used in residue analysis in function of time.

Next to the improving detection capability of the instrumentation also the clean-up of the samples prior to instrumental analysis has undergone an evolution in function of time. As a general rule the results of the instrumental technique are correlated strongly with the efficacy of the clean-up. While in the 70s only solvent extraction and homemade columns (e.g. Silicagel, AlO) were used for clean-up, solid-phase extraction (SPE; 80s), immuno affinity chromatography (IAC; 90s) and molecular imprinted polymers (MIPs; end 90s) took over the job. HPLC fractionation, also often used, results in several purified fractions each containing a limited number of analytes and matrix components. In that aspect comprehensive (two-dimensional) GC or LC prior to MS may be important in the future.

Next to clean-up and analysis, the knowledge of the metabolism of A and B substances is important. Often not the parent (original) substances have to be detected but also one or more metabolites, depending upon the matrix analysed. Animal experiments are needed for those purposes but also some alternatives have been described [6,7].

In this review literature is retrieved from different sources over a period of ca. 35 years. Next to the traditional peer-reviewed a1 journals in which residue chemists publish also the proceedings of the two main Benelux conferences in the field: "Euroresidue" (six editions) and the international conference on hormone and veterinary drug residue analysis "the Ghent conference" (seven editions) were used.

The analytical method and its performance must always be seen in the light of the interpretation of the analytical result. Food inspection services are interested mainly (only?) in YES/NO answers: has this animal been treated illegally? Is the concentration of the residue higher than a certain value (MRL), etc.? In fact all questions may be resumed to one major question: is the sample compliant or is the law violated? When the answer to that last question is YES, legal actions have to be taken. Therefore the analytical results must be accurate "beyond any reasonable doubt".