A Review of Veterinary Drug Residue Detection: Recent Advancements, Challenges, and Future Directions

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Abstract: Veterinary drug residues of common food (milk, meat) have posed serious threats to the environment and human health, making the quality and safety of agricultural, livestock, and aquatic products increasingly prominent. With the widespread use of veterinary drugs and the requirements for food safety, it has become urgent to detect veterinary drug residues in animal-derived foods. So far, few studies have systematically reviewed the progresses, challenges, and future directions in veterinary drug residue detection. A thorough review on the current advancements, challenges, and potential future directions of veterinary drug residue detection will be extremely beneficial and timely. This study reviewed recent developments of detection technology of veterinary drug residues. The current issues and challenges in veterinary drug residue detection were examined and highlighted. Finally, future proposals on directions and prospects for veterinary drug residue detection were suggested. High-throughput and high-sensitivity veterinary drug detection technology, sample pretreatment technology for rapid processing, and the fusion of multiple detection methods were recommended as the main directions for the future development of veterinary drug residue detection. It was suggested to develop the analysis and detection technologies of veterinary drug residue towards high automation, high sensitivity, and high throughput in the future. This review provides new ideas and strategies for the rapid development of animal husbandry industry and protecting consumers’ physical health and food safety.

Keywords: veterinary drug; residue; pretreatment technology; detection technology

1. Introduction

Globally, due to continued population expansion and a shift in diet toward meat eating, the demand for animal-derived food has significantly increased [1]. The output of animals has grown quickly to sustain food security [2,3]. Veterinary drugs, including antiparasitics, antibiotics, and growth promoters, are crucial for preserving the wellbeing and production of agricultural animals, and the health of companion animals [4]. As veterinary drugs are frequently used to enhance animal development and to prevent sickness in food-producing animals, there may be drug residues in foods such as meat, milk, eggs, or honey [5–7]. Veterinary drug residues refer to the residues of veterinary drug parent compounds or metabolites contained in any edible part of animal products, as well as impurities related to veterinary drugs [8]. They are one of the most important pollution sources from animal foods and are tightly connected with the animal food safety. Drug residues from animal foods not only cause serious consequences such as acute poisoning, allergic reactions, bacterial resistance, human flora imbalance, carcinogenesis, teratogenicity, and mutagenicity, but also lead to enormous losses in the national economy [9,10]. Controlling veterinary drug residues strictly and enhancing detection techniques, especially quick, sensitive, accurate, and easy testing techniques, are of great significance for preserving ecological ecosystems and maintaining human health [1,10].
The monitoring and controlling of veterinary drug residues are essential for the research, development, use, and management of veterinary drugs at home and abroad. Various countries and international organizations have stipulated their drug withdrawal periods and maximum residue limits (MRLs), and China has also imposed strict restrictions. Maximum permissible amounts for veterinary drug residues are defined by the Food and Drug Administration (FDA) in the USA. Maximum residue limits (MRLs) are made public by the European Medicines Agency (EMA) in the European Union (EU). The majority of developing nations use EU or Codex MRLs [9]. In order to achieve regulatory objectives, effective detection methods are essential [11].

Various detection methods have been used to evaluate veterinary drug residues [11–14]. For instance, Zhao et al. [11] fabricated a uniform 2D SERS-active plasmonic metal NP-CsPbX3 hybrid films to study the effects of different CsPbX3 QDs on SERS activity of hybrid films based on the detection of multiple veterinary drug residues. Stolker et al. [12] performed the target analysis with low concentrations of 25 µg/kg dexamethasone in feed by combining liquid chromatography (LC) and immunoaffinity chromatography (IAC) with ultraviolet (UV) detection. Kaufmann et al. [14] proposed a method covering more than 100 different veterinary drugs based on a single stage orbitrap mass spectrometer operated at 50,000 FWHM, which was validated in muscle, kidney, liver, fish, and honey according to the EU Commission Decision 2002/657/EEC. Existing reviews on veterinary drug residue detection tend to focus on either progressive technologies or practices experience various aspects [15–20]. Despite these review and overview efforts, to the best of our knowledge, few studies have systematically reviewed the progresses, challenges, and future directions in veterinary drug residue detection. Moreover, veterinary drug residue detection has witnessed more rapid developments and advances in the last decade. In order to accelerate the scientific, institutionalized, and standardized processes of veterinary drug management, a comprehensive review on the recent advancements, challenges, and future directions of veterinary drug residue detection will be quite timely and valuable.

Here, this review is arranged as follows: Section 2 introduces the recent advancements of detection technology of veterinary drug residues; Section 3 analyses the existing problems and challenges in veterinary drug residue detection; and Section 4 proposes the future directions for veterinary drug residue detection. This review provides new ideas and strategies for the rapid development of animal husbandry industry.

2. Recent Advancements in Detection Technology for Veterinary Drug Residues

In a complete experimental process, the sample pretreatment is the key to the detection of veterinary drug residues, accounting for the largest proportion of time. The pretreatment processes of samples include extraction, purification, concentration, or derivatization. In detecting veterinary drug residues, complex matrices such as water, protein, and fat can increase the difficulties of separation and purification, affecting the purification effect and the speed of drug to be tested. Therefore, it is necessary to select appropriate pretreatment methods for detecting different samples. Currently, commonly used sample pretreatment techniques for detecting veterinary drug residues include liquid–liquid extraction, solid-phase extraction, QuECHERS, and accelerated solvent extraction. Detection analytical techniques for veterinary drug residues are mainly composed of gas chromatography–mass spectrometry, liquid chromatography, liquid chromatography–mass spectrometry, capillary electrophoresis, immunoassay, and biosensor analysis. The advantages and disadvantages of sample pretreatment and detection analytical techniques are shown in Table 1.
Table 1. Comparison of advantages and disadvantages of different detection methods for veterinary drug residues.

<table>
<thead>
<tr>
<th>Method</th>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td>Liquid–liquid extraction [21,22]</td>
<td>• Simple operation</td>
<td>• Large workload</td>
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<td></td>
<td>• Good separation effect</td>
<td>• Volatile</td>
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<td></td>
<td>• High applicability</td>
<td>• Toxic extraction solvent</td>
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<tr>
<td>Solid-phase extraction [23,24]</td>
<td>• Good purification effect</td>
<td>• High solid-phase extraction column cost</td>
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<td></td>
<td>• Strong selectivity</td>
<td>• Large recovery error</td>
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<td></td>
<td>• Short separation time</td>
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<td></td>
<td>• Low solvent consumption</td>
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<tr>
<td>QuEChERS [25,26]</td>
<td>• Flexible</td>
<td>• Insufficient purification effect</td>
</tr>
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<td></td>
<td>• Effective</td>
<td>• Susceptible to matrix interference</td>
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<td></td>
<td>• Low reagent consumption</td>
<td></td>
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<tr>
<td></td>
<td>• Wide analysis range</td>
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<tr>
<td>Accelerated solvent extraction [27,28]</td>
<td>• Safe and fast</td>
<td>• The need for high temperature</td>
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<tr>
<td></td>
<td>• High extraction efficiency</td>
<td>• The need for pressure</td>
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<td></td>
<td>• Small matrix effect</td>
<td>• The need for complex instrument operation</td>
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<td></td>
<td>• Automatic batch processing</td>
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<tr>
<td>Gas chromatography–mass spectrometry [29,30]</td>
<td>• Fast detection speed</td>
<td>• Mainly suitable for the detection of small-molecular-weight drugs that can be vaporized or derived and can be vaporized</td>
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<tr>
<td></td>
<td>• High sensitivity</td>
<td>• The signal output after detection needs to be corrected</td>
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<td></td>
<td>• Low detection costs</td>
<td></td>
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<tr>
<td>Liquid chromatography [31,32]</td>
<td>• High separation efficiency</td>
<td>• High analysis and detection costs</td>
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<td></td>
<td>• Good selectivity</td>
<td>• Expensive prices</td>
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<td></td>
<td>• High detection sensitivity</td>
<td>• Expensive routine maintenance costs</td>
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<tr>
<td></td>
<td>• Automatic operation</td>
<td>• Long analysis time</td>
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<tr>
<td></td>
<td>• Wide application range</td>
<td></td>
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<tr>
<td>Liquid chromatography–mass spectrometry [33–35]</td>
<td>• Wide group analysis range</td>
<td>• Strong polarity</td>
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<td></td>
<td>• Strong separation ability</td>
<td>• Lacking suitable ionized functional groups</td>
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<td></td>
<td>• Reliable results</td>
<td>• Difficult to directly detect</td>
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<tr>
<td>Capillary electrophoresis [36,37]</td>
<td>• Simplicity and rapidity</td>
<td>• Small injection volume</td>
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<td></td>
<td>• High precision</td>
<td>• Insufficient preparation ability</td>
</tr>
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<td></td>
<td>• Low reagent consumption</td>
<td>• Limitations in reproducibility</td>
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<tr>
<td></td>
<td>• High separation efficiency</td>
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<td>Immunoassay [38–44]</td>
<td>• High specificity</td>
<td>• Determine only the protein content of cytokines</td>
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<td></td>
<td>• Simple and fast operation</td>
<td>• The results are strongly related to the source and affinity of the antibody used</td>
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<td></td>
<td>• Relatively few influencing factors</td>
<td>• Relatively low sensitivity</td>
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<td></td>
<td>• Good repeatability</td>
<td>• The presence of soluble receptors for cytokines in the sample may affect the binding of specific antibodies to cytokines</td>
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<td></td>
<td>• Easy to standardize</td>
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<tr>
<td>Biosensor analysis [45,46]</td>
<td>• Using immobilized bioactive substances as catalysts</td>
<td>• Highly experimental in the early stage</td>
</tr>
<tr>
<td></td>
<td>• Strong specificity</td>
<td>• Poor stability</td>
</tr>
<tr>
<td></td>
<td>• Fast analysis speed</td>
<td>• Poor reproducibility</td>
</tr>
<tr>
<td></td>
<td>• High accuracy</td>
<td></td>
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<td></td>
<td>• Easy to operate</td>
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<td></td>
<td>• Low cost</td>
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2.1. Sample Pretreatment Technology

2.1.1. Liquid–Liquid Extraction

The liquid–liquid extraction method is one of the most classical extraction and purification methods. Its principle is to use the solubility difference between the components to be measured and the sample impurities in two immiscible phases for purification. It is
widely used in extracting substances with similar properties to be measured. Imamoglu and Olgun [21] used ethyl acetate containing 0.1% acetic acid for liquid–liquid extraction to detect 26 veterinary drugs and 187 pesticide residues in milk, and obtained satisfactory results. Li et al. [22] extracted 25 veterinary drugs from milk with acetonitrile based on liquid–liquid extraction method, resulting in a small matrix effect and satisfactory recovery.

2.1.2. Solid-Phase Extraction

Solid-phase extraction refers to the separation of solutes after achieving a distribution equilibrium between a polymer fixed-liquid membrane and an aqueous solution. This method can absorb the target substance in a liquid sample using a solid adsorbent, followed by elution or thermal desorption, to achieve the purpose of separating and enriching the target drug. Melekhin et al. [23] developed a magnetic solid-phase extraction procedure using magnetic hyper-cross-linked polystyrene (HCP/Fe₃O₄) for the sample preparation of 132 veterinary drugs. Casado et al. [24] used liquid–solid extraction and a solid-phase extraction procedure for treated meat samples to determine 23 veterinary drug residues (β-blockers, β-agonists, and non-steroidal anti-inflammatory drugs).

2.1.3. QuEChERS

The QuEChERS extraction method is named for its fast, simple, inexpensive, effective, stable, and safe characteristics. Its principle is to use the interaction between the adsorption filler and impurities in the matrix to adsorb impurities, thereby achieving purification. Stubbings and Bigwood [25] developed a new sample preparation procedure loosely based on QuEChERS methodology to screen whether there were veterinary drug residues in animal tissues. They pointed out that this method was also applicable to macrolide and lincosamide antibiotics, benzimidazoles, levamisole, avermectins, and tranquillizers. Kang et al. [26] extracted 66 veterinary drugs from beef and milk using the QuEChERS method. They found that within the concentration range of the experiment, the recovery rate of all veterinary drugs was above 70.0%, and other quality parameters all met the detection requirements.

2.1.4. Accelerated Solvent Extraction

Accelerated solvent extraction is a technology for automated extraction of solid or semi-solid samples using organic solvents under high temperature and pressure. High temperature can increase the solubility of analytes and reduce matrix effects. High pressure can maintain the solvent in a liquid state at high temperatures, ensuring that volatile substances do not volatilize, and reducing extraction time. This method is fast, accurate, and highly sensitive. Han et al. [27] combined accelerated solvent extraction with gel permeation chromatography to detect clotrimazole residues in beef and bovine kidney. Yu et al. [28] developed an accelerated solvent extraction method for extracting seven tetracycline compounds from beef and liver, and the trichloroacetic acid/acetonitrile was extracted at a temperature of 60 °C and a pressure of 65 bar.

2.2. Detection Analytical Techniques

2.2.1. Gas Chromatography–Mass Spectrometry (GC–MS)

Gas chromatography separates the mixtures based on the different rates at which the compounds to be tested pass through the chromatographic column driven by the carrier gas. Generally, the detection of drug residues by gas chromatography requires a derivatization reaction, and selects a specific capillary column to separate the sample, which is connected to a mass spectrometry detector for analysis and determination. Although GC–MS has fast detection speed and high sensitivity, it is mainly suitable for the detection of small-molecular-weight drugs that can be vaporized or derived and can be vaporized. For some unstable or large-molecular-weight drugs, other detection methods can only be selected. Na et al. [29] used liquid and gas chromatography coupled with mass spectrometry to detect pesticides, veterinary drugs, and mycotoxins in feed. They revealed the recovery
rate was between 70.09% and 119.76%, and the relative standard deviations were less than or equal to 18.91%. Kumar et al. \[30\] optimized a multiresidue method for the simultaneous analysis of multiple insecticides and some commonly used veterinary drugs based on LC–MS/MS and GC–MS/MS, effectively minimizing the matrix interferences. Their results indicated that the limit of quantification (LOQ) was 0.01 mg/kg, and the recoveries at LOQ and higher levels ranged between 70% and 120%, with the RSDs precision of less than 20%.

2.2.2. Liquid Chromatography (LC)

LC uses liquid as the mobile phase. It allows a single solution of various polarity to pass through or a mixed solution of several substances to cross through a stationary phase chromatographic column using a high-pressure infusion system. The purpose of separation and detection is to achieve different retention times through the chromatographic column. HPLC and UPLC are detection techniques developed on the basis of liquid chromatography, characterized by high speed, efficiency, and sensitivity. Currently, they are commonly used for detecting veterinary drug residues in beef, mutton, and cow and goat milk. After separating the target compound by liquid chromatography, suitable detectors should be selected for determination. For example, fluorescence detectors are suitable for drugs that possess or derive fluorescent groups, while diode array detectors and ultraviolet detectors need to rely on ultraviolet groups for detection. Also, there is an increasing need for LC applications in food and environmental areas that are able to cope with a large number of analytes in very complex matrices \[31\]. Boix et al. \[32\] applied a LC screening method to finish qualitative validation for 116 drugs in different animal feeds at 0.02 and 0.2 mg kg\(^{-1}\). Their findings suggested that an investigation of 22 commercial feeds revealed numerous promising results, including the presence of prohibited \(\alpha\)- and \(\beta\)-nandrolone.

2.2.3. Liquid Chromatography–Mass Spectrometry (LC–MS)

LC–MS uses liquid chromatography as the separation system and mass spectrometry as the detection system. Due to the strong qualitative ability of mass spectrometry, it has been widely applied in the field of organic matter analysis. Nowadays, the commonly used LC–MS methods for detecting veterinary drug residues in beef, mutton, and cow and goat milk include HPLC–MS/MS and UPLC–MS/MS, which have the advantages of wide analysis range, strong separation ability, and reliable results \[33\]. Castilla-Fernández et al. \[34\] developed an ultra-high-performance liquid chromatography–tandem mass spectrometry method to analyze various pesticides and veterinary drugs in fatty fish samples. They obtained a negligible matrix effect for 57% of the studied compounds and more than 20% precision in all cases. León et al. \[35\] established a QuEChERS-based extraction method, and coupled an ultra-high-performance liquid chromatography with high-resolution mass spectrometry (UHPLC–HRMS) for 77 banned veterinary drugs and a post-target screening for 425 substances. They presented recoveries ranging from 80 to 120%, with a precision in terms of relative standard deviation (RSD) lower than 20%.

2.2.4. Capillary Electrophoresis (CE)

CE is a technology that utilizes electroosmosis as a driving force to achieve separation under high voltage and direct current electric fields and capillary tubes as the separation channels, depending on the passing speed of each sample component. The CE method has the advantages of simplicity, rapidity, high precision, low reagent consumption, and high separation efficiency. However, due to the small injection volume, the preparation ability is insufficient, and there are certain limitations in reproducibility. Kowalski et al. \[36\] proposed a CE method with UV detection for the quantitative determination of residues from poultry and porcine tissues. Their results showed that this method was able to identify drug residues in tissues at level below 20 microg/kg. Yang et al. \[37\] revealed that the LOD of milk samples was between 1.8 \(\mu\)g L\(^{-1}\) and 16.3 \(\mu\)g L\(^{-1}\) through CE analysis of six sulfonamides in livestock products.
2.2.5. Immunoassay

An immunoassay is a simple and fast method for determining and analyzing target compounds through specific binding of antigens and antibodies after immune reactions [38]. An immunoassay is more suitable for the qualitative testing of large batches of samples, and its development requires ensuring accuracy and sensitivity to avoid the “false positive” problem. A variety of immunoassays are increasingly applied in the detection of veterinary drug residues because they are fast, simple, and cheap. Traditionally, there are three immunoassays, including an enzyme-linked immunosorbent assay (ELISA) [39,40], a lateral flow immunoassay (LFI) [41,42], and a chemiluminescence immunoassay (CLI) [43,44]. For instance, Byzova et al. [41] carried out rapid qualitative and quantitative control of the veterinary drug bacitracin in milk based on the lateral flow immunoassay method. The thresholds for visual and instrumental detection of bacitracin using the developed assay are between 100 ng/mL and 1.0 ng/mL. They also found the average error of measurement was in the range of 1.5~7.0%, and the assay of milk samples was implemented in 10 min without any pretreatment.

2.2.6. Biosensor Analysis

With the maturity of nanotechnology, the development of biosensor technology has provided a new direction for the detection of veterinary drug residues in mutton, cattle, and cow and goat milk. Green, environmentally friendly, safe, and effective high-sensitivity detection methods have great potential for future development. Biosensors have the advantages of low reagent consumption, high sensitivity, and saved time and labor. However, their applications in residue detecting in beef, mutton, and cow and goat milk are not very widespread. Currently, they are mainly used to detect the quality and flavor of meat. Due to the short research history, there are still many problems to be solved. With the deepening of related research, the application of this method in the field of veterinary drug residue detection will become a trend. Sun et al. [45] detected tetracycline veterinary drug residues in milk samples by applying chemiluminescence sensor method. Wang et al. [46] used electrochemical sensors to detect chloramphenicol residues in samples. They demonstrated that this method had high sensitivity, good repeatability, and stability, and had been successfully used for the detection of chloramphenicol in milk samples.

3. Challenges in Veterinary Drug Residue Detection

3.1. Few Applications of New Sample Pretreatment Technologies

The residue detection of veterinary drugs in animal-derived foods mainly includes sample pretreatment and detection analysis. Due to the complex composition of animal-derived foods, the significant substrates impact, and the relatively trace amounts of veterinary drug residues contained therein, it is difficult to isolate and purify various veterinary drug residues from animal-derived foods. Consequently, sample pretreatment is crucial for the detection of veterinary drug residues, which can directly affect the accuracy of the analytical results of veterinary drug residues [47]. Currently, the commonly used sample pretreatment techniques for detecting veterinary drug residues include liquid–liquid extraction, solid-phase extraction, QuEChERS, and accelerated solvent extraction. These existing processing technologies have their own shortcomings (Table 1). However, some new sample pretreatment technologies with faster processing speed are relatively rarely applied, especially in the residue of multiple types of veterinary drugs, such as stir bar sorption extraction (SBSE) [48,49], molecular imprinting technology [50,51], and immunoaffinity chromatography (ICA) [52,53], and so on.

3.2. Less Multi-Residue Detection Methods

For multiple residue detection methods for the same type of veterinary drugs, the relevant research mainly focuses on fluoroquinolones (FQs) and sulfonamides (SAs) in the domestic and foreign literatures [54,55]. FQs, generally with fluorescence characteristics, can be detected by HPLC–FLD method directly, while SAs with poor fluorescence can be
detected by a precolumn derivatization fluorescence method. In addition, for multiple residue detection methods for the different types of veterinary drugs, different types of veterinary drugs generally have different polarities and chemical properties, making it difficult to simultaneously extract, purify, and detect multiple types of veterinary drug residues. Currently, there are few examples of them in the literature, mainly for the detection of some antibiotics. For example, Schneider et al. [54] used the HPLC–FLD method to simultaneously detect five FQs and three tetracycline veterinary drugs in chicken, with a detection limit of 0.5 to 5 ng/g. Stubbins et al. [55] used the ion exchange solid-phase extraction column–HPLC method to detect SAs, imidazoles, FQs, and other drugs in animal tissues, with the recoveries of 53–104%. The popularization of high-efficiency and high-resolution large-scale instruments have improved the sensitivity and accuracy of veterinary drug residue detection. Currently, multi-residue detection methods are developing towards sensitivity, speed, accuracy, efficiency, and simplicity of operation. The continuous emergence of new technologies and the widespread penetration of various disciplines have important roles in multi-residue detections, ensuring animal food safeties and promoting healthy developments of animal husbandry.

3.3. Lack of High and New Detection Technology

There are many modern biological techniques that can be used in the detection of veterinary drug residues, with overall high sensitivity and reliability. However, it is still necessary to select specific immune antibodies, enzymes, and adaptors based on the type of substance to be tested in order to ensure the detection effect. In recent years, the application of quantum dot technology has made significant progress in the qualitative and quantitative analysis of veterinary drug residues, further promoting the wide application of new technologies for testing livestock products, such as quantum dot labeling immune technology [56–58], quantum dot sensor technology [59–61], quantum dot molecular imprinting technology [62–64], quantum dot self-assembled film technology [65], and quantum dot fluorescence probe technology [66]. However, at present, the application of quantum dots combined with immunochromatography is relatively rare. In addition, although the new technologies of quantum dots have solved some drawbacks of traditional methods, such as instrumental detection in testing agricultural and veterinary drug residues, it still needs to be improved in some aspects, such as the preparation of water-soluble quantum dots, the coupling of quantum dots with biological macromolecules, and so on.

4. Future Directions of Veterinary Drug Residue Detection

4.1. High-Throughput and High-Sensitivity Veterinary Drug Detection Technology

With the continuous progress of detection technology, it is urgent to develop more sensitive and operational detection technology for veterinary drug residues. At present, some coupled technologies of immunoassay, spectroscopy, and chromatography have been greatly developed, improving the detection abilities for veterinary drug residues. In addition, some emerging technologies are widely used. For example, the nanotechnology is no longer a concept or a theory of the new world, and it has turned into a new enabling technology over the years. Nanotechnology has a great potential for solving many problems related to animal health, production, reproduction, and effective hygienic practices related to livestock production [67,68].

The time-resolved fluorescence immunoassay (TRFIA) recommended by the WHO is a nonradioactive labeling immunoassay technique that uses lanthanide elements such as europium (Eu), terbium (Tb), samarium (Sm), and niobium (Nd) as markers. Many of its advantages come from the inherent characteristics of lanthanide ion chelates. When excited by ultraviolet light, nitrogen laser, or xenon lamp, lanthanide ion chelates emit fluorescence. TRFIA has the characteristics of low background interference, high sensitivity, strong specificity, and high accuracy. In particular, the characteristics of multi-labeling and multi-signal measurements are unique in current labeling technology. Using the difference in fluorescence wavelength and fluorescence decay time between different lanthanide ions,
it introduces two or more lanthanide ion markers, and simultaneously detects multiple substances in the sample through time-resolved fluorescence measurement. The emergence of this biotechnology, with broad development potential, will bring a revolution in the detection of trace pollutants in agricultural products and food. In the future, developing the micro, fast, convenient, and high-throughput technologies is the direction of veterinary drug detection [69,70].

4.2. Sample Pretreatment Technology for Rapid Processing

Sample pretreatment technology is a key step in the detection of veterinary drug residue. With the intensive development of aquaculture scale, the number of veterinary drugs and additives has increased, resulting in increased difficulty in detection. Establishing rapid pretreatment methods of sample processing can improve the efficiency of sample analysis, save the solvent and sample consumption, and improve the detection ability for veterinary drugs residues. Moreover, it can also reduce the impact of veterinary drug residues, and avoid the inflow of products with excessive pesticide and veterinary drugs into the market, providing advanced technical support for agricultural regions, food processing plants, markets, and other places. Several studies have aimed to develop a general optimized method for analysis of multi-analyte samples [71–73]. Microwave-assisted extraction (MAE) is a new sample pretreatment method, offering many advantages such as the combined reduction in the extraction time, and solvent and energy consumptions, as well as the possibility of performing simultaneous multiple extractions, thus, increasing the number of samples processed daily [74].

Classical sample pretreatment methods are not only cumbersome and time-consuming in operation, but also inefficient in extraction and purification, and require the use of a large number of toxic solvents. In addition, due to the increasingly low requirements for the minimum detection limit of the tested target substance, the stability of its target substance is also changing over time, which brings certain difficulties to analysis and testing. In the future, sample pretreatment technology will develop towards simplicity, efficiency, high selectivity, low sample consumption, low reagent consumption, automation, and suitability for multi-residue detection.

4.3. Fusion of Multiple Detection Methods

Currently, the main detection methods for multiple residues of veterinary drugs include instrumental analysis and immunoassays. Instrumental analysis has high sensitivity and accuracy, which is essential as a confirmatory method. However, the instruments and equipment used in this method are expensive, cumbersome, time-consuming, and require professional operators. The complex pretreatment cannot achieve rapid detection, which, to some extent, limits its popularity and application. An immunoassay has the advantages of sensitivity, rapidity, and high-throughput screening optimization, and has become an important method for the detection of multiple residues of pesticides. However, current analytical methods are very immature, and problems such as stability, sensitivity, and repeatability have not been well resolved.

Integrating the use of old and new technologies, such as liquid chromatography–ultraviolet detection technology [75], high-performance liquid chromatography–fluorescence detection technology [76], liquid chromatography–mass spectrometry detection technology [77], high-resolution mass spectrometry detection technology [78], and enzyme-linked immunosorbent detection technology [79], as well as nanotechnology [68] and multi-channel automated detection technology applications [80], can effectively improve flux analysis and detection sensitivity. It can effectively improve the effectiveness and quality of detecting veterinary drug residues. Especially in plant- and animal-derived foods, the comprehensive use of these technologies can greatly improve the effectiveness and quality of detecting veterinary drug residues. Due to the diversities of animal-derived food substrates and the differences in veterinary drug residues in samples, developing multiple detection methods for veterinary drug residues is urgent, especially for animal-derived
foods with multiple substrates, which have gradually become the main development trend in veterinary drug residue detection.

5. Conclusions

This paper reviews the recent advancements, challenges, and future directions of veterinary drug residue detection. The recent developments in detection technology of veterinary drug residues at home and abroad are introduced in detail. However, the problems and challenges in veterinary drug residue detection are still existing, such as few applications of new sample pretreatment technologies, less multi-residue detection methods, and lack of a fusion of old and new detection technology. In order to achieve the goals of the screening, measurement, and confirmation processes, while concurrently detecting different kinds of veterinary drugs, in the future, the primary development directions for veterinary drug residue detection should focus on high-throughput and high-sensitivity veterinary drug detection technology, sample pretreatment technology for quick processing, and the fusion of several detection technologies.

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