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A comprehensive review of the analytical methods reported for the assay of two veterinary drugs in different matrices

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ABSTRACT

These studies are devoted to developing novel analytical methods to assay levofloxacin and florfenicol in different matrices; dosage forms, milk products, meat, and biological fluids. Veterinary drugs are consumed on a large scale, whether administered as food additives or added to drinking water. Besides, these pharmaceuticals are provided for animals as a prophylactic agent, to treat different diseases and to enhance their growth. Veterinary drug residues in food are a significant concern, and their detection, prevention, and management are crucial to ensure food safety and protect consumer health. Therefore, for public health concerns, regulatory authorities have established guidelines to control the limit of veterinary residues in animals and their different food products. This current review involves various methods that have been published to determine different veterinary drugs, including; spectrophotometry, electrochemical methods, and different chromatographic methods. All suggested methods are fully validated under the guidance of International Conference of Harmonization to be suitable for application of the developed methods for their intended purpose.

Keywords: veterinary drugs, review, regulatory authorities, analytical methods

1. Introduction

Veterinary drugs (VDs) play a crucial role in the healthcare of livestock , as they are prescribed to cure animal diseases and control infections **(Mouiche et al., 2019).**These agents have been shown to improve animal production efficiency, enhance livestock product quality, and contribute to the maintenance of ecological balance **(Teng et al., 2023)** . Studies have demonstrated that the use of VDs in animal farming can increase feeding and performance,

resulting in higher agricultural productivity **(Baars, 1984)**.However, the benefits of drug administration to farm animals used for food production are also accompanied by the risks associated with drug residue in the edible parts of animal tissues **(Moreno et al, 2017)**.As highlighted in various sources, the illegal and abusive usage of VDs can result in both short-term and long-term public health hazards **(Canton et al., 2021)**.These drugs can be accumulated in animal tissue and the residues can cause severe risks to human health, such as toxic effects and allergic reactions. Another consequence is the development of resistant bacteria, which might interfere with the efficiency of veterinary drugs and even difficult disease treatment **(Canton et al., 2021)**

Nowadays, many classes of antibiotics (ABs), such as amphenicol and quinolones are widely used for promoting growth and feeding in food-producing animals. Moreover, some of the ABs can be added directly to food, mainly to the milk to prolong its freshness **(Sachi et al., 2019).**Amphenicols are classes of broad-spectrum antibiotics, including chloramphenicol and florfenicol. The mechanism of action of these pharmaceuticals involves inhibiting the bacterial

growth by binding to the bacterial ribosome and inhibiting protein synthesis **(Shaw & Leslie, 1991)**. Florfenicol (FLR) is a third-generation product of chloramphenicol with low toxicity and is

commonly used to treat animal diseases **(Bryskier, 2005)**. It is chemically designed as 2,2-dichloro-N-[(1R,2S)-3-fluoro-1-hydroxy-1-(4-methanesulfonylphenyl)propan-2-yl]acetamide (Figure 1) **(Sweetman, 2005)**.

Quinolones (QLs) are broad-spectrum antibiotics and have been used in the treatment of various bacterial infections such as urinary tract infection, respiratory tract infection, skin and soft tissue infections **(Fàbrega et al., 2009).** They work by targeting bacterial DNA gyrase and topoisomerase IV, which are essential enzymes in the replication and repair of bacterial DNA **(Fàbrega et al., 2009).**

Synthetic fluoride containing derivative quinolones, such as levofloxacin (LEV), is a member of fluoroquinolone group that shares a bicyclic core structure **(Baggio & Ananda-Rajah, 2021)**. It is effective against gram- negative and gram-positive bacteria and chemically denoted as: (S)-9-Fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H-pyrido[1,2,3-de]-1,4- benzoxazine-6 carboxylic acid (Figure 2) **(Sweetman, 2005)**.

Several analytical approaches have been developed to determine those antibiotics in their pure form, pharmaceutical formulations, and biological materials. This review article provides a detailed summary of the analytical approaches available for evaluating FLR and LEV as veterinary residues in various matrices.

1. Review of analytical approaches

2.1. Spectrophotometric methods.

Various spectrophotometric methods have been mentioned before for determining FLR and LEV in both bulk and pharmaceutical formulations. These methods are listed in Tables 1 and 2respectively.

2.2. Chromatographic methods

Various chromatographic methods, such as HPLC with UV detection, UPLC and TLC havebeen reported and optimized for determination of FLR and LEV as veterinary residues in different samples. These methods are outlined in Tables 3 and 4, respectively.

2.3. Electrochemical methods

2.3.1. For Florfenicol

A Dendritic pt-pd nanoparticles -modified glassy carbon electrode was developed. This sensorshowed excellent response for the concerned drug in the linear range of 5.0×10^{-8} - 8.0×10^{-6} mol L^{-1} with a detection limit of 1.0×10^{-9} mol L^{-1} **(Fan et al., 2020).** Another electrochemical behaviour depends on a poly(3-methylthiophene)- modified electrode as a voltametric sensor for sensitive detection of FLR **(Taşkın et al., 2021)**.

2.3.2. For levofloxacin

An electrochemical sensor for LEV detection was developed by electrochemical polymerization of pyrogallol red (PGR) on the glassy carbon electrode **(Koçak et al., 2022).** A potentiometric estimation of LEV using a nano-sized silica carbon past electrode was constructed. It showed great electrocatalytic activity in the oxidation of 1.0 mM LEV in Britton–Robinson buffer (BR) at pH values ranging from 3.0 to 8.0 **(Fekry, 2022).**

Conclusion

Based on analytical study reports, the current review provides an overview of several techniques and procedures used in the quantification of veterinary residues, such as FLR and LEV. The review would give analytical chemists significant insights, allowing them to understand the fundamental solvents and their respective combinations suitable for the instruments used in the analytical laboratory. Analytical chemists can learn about the advantages and disadvantages of various techniques by studying comparative data offered in published scientific literature.

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Disclosure

The authors report no conflicts of interest in this work

Table 1: Reported spectrophotometric methods for determination of FLR.

Matrix	Assay conditions	Selected wavelength (λ_{max})	Ref
Pure and pharmaceutical formulations	First derivative spectrophotometric determination of FLR in alkaline solution.	274 nm	(Mohammed M Elimam et at.,2016)
Bulk and pharmaceutical formulation	Zero, first and second derivative spectrophotometric determination of FLR in aqueous solution	274 nm and 281 nm	(Mohamed M Elimam et al., 2016)

Table 2: Reported spectrophotometric methods for determination of LEV.

Matix	Assay conditions	Selected wavelength (λ_{max})	Ref
Pure and pharmaceutical formulations	Direct determination of LEV in 0.1M HCl	290 nm	(Desai, et al., 2011)
Bulk and market formulation	Direct determination of LEV in diluent composed of water: methanol: acetonitrile; (9:0.5:0.5,*v/v/v*)	292 nm	(Maleque et al., 2012)

Table 3: Reported chromatographic methods for determination of FLR.

Sample	Stationary phase	Mobile phase	Detection	Ref
Medicated feeding stuffs	Phenyl column C6	Different ratio of the gradient mobile phase consisting of water: acetonitrile with time programming	UV detection at 223 nm	(Patyra & Kwiatek, 2019)
Fish	C18	0.05M ammonium acetate: acetonitrile: tetrahydrofuran;(76:23:1,*v/v*) at pH=7.2	UV detection at 223 nm	(Hung et al., 2019)
Milk	C18	Water: acetonitrile;(75:25, *v/v*)	UV detection at 224 nm	(Karami-Osboo et al.,2016)
Bovine tissue	ODS-4	Different ratio of gradient mobile phase consisting of 0.1% acetic acid: acetonitrile with time programming	MS/MS	(Saito-Shida et al., 2019)
Egg	C18	Different ratio of gradient mobile phase consisting of 1% formic acid: methanol with time programming	MS/MS	(Li et al., 2022)
Porcine edible tissue	Silica gel (60 GF_{254} glass plate)	Consisting of ethyl acetate: acetone: ammonium hydroxide;(2:8:0.5,*v/v/v*)	Densitometric detection at 225 nm	(Zhou et al., 2020)
Veterinary formulation and milk	Fused silica capillary with 50 µm internal diameter	1 mM borate buffer at pH 9.3	UV detection at 224 nm	(Aboul-Enein, Wagdy, & Bowser, 2019)

Table 4: Reported chromatographic methods for determination of LEV.

Sample	Stationary phase	Mobile phase	Detection	Ref
Fruits and leafy vegetables	C18	Different ratio of gradient mobile phase consisting of 0.05% formic acid: acetonitrile with time programming	MS/MS	(Merlo et al., 2022)
Biomimetic media	C18	Acetonitrile: water;(15:85, *v/v*) at pH 3	UV detection at 284 nm	(Matos et al., 2017)

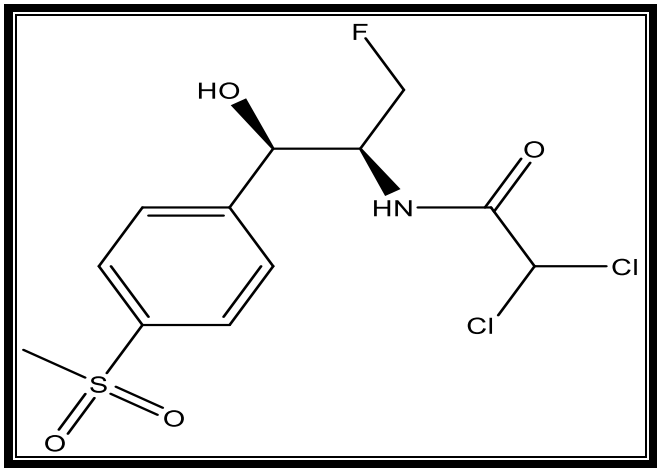

Figure 1

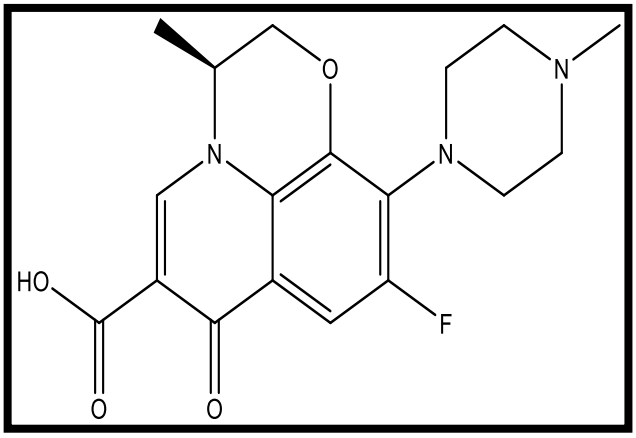

Figure 2

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