



Bioanalytical Approaches for Analysis of Triclabendazole as Veterinary Residue in Different Matrices

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Abstract

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Anthelmintics drugs are used to treat infectious diseases in the intestinal tract of animals caused by parasitic worms. These drugs are important in the livestock industry for controlling coccidiosis, a parasitic disease that can have significant economic impacts. The excessive use of these agents in the poultry and livestock industries, and their continuous use has led to the development of resistance in the parasites they target. 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 concern, regulatory authorities have established guidelines to control the limit of veterinary residues in animals and their different food products. Sample preparations and analytical techniques are crucial for detecting veterinary medication residues in foods generated from animals, maintaining food safety. Various extraction methods such as LLE, SPE and MSPD are used for the determination of veterinary drug residues, and analytical techniques like spectroscopic and chromatographic methods are employed for this purpose.

Keywords: Anthelmintics; resistances; triclabendazole; veterinary residues.

1. Introduction

Animals need veterinary drugs extensively to cure illnesses, encourage growth, and increase feeding efficiency. Moreover, the use of food producing animals may leave residues of the parent compounds or their metabolites in food products resulting in dangerous effects to humans. For this reason, sensitive and selective analytical methods

have been developed and optimized for ensuring the food safety. (Wang, Xie, & Lee, 2021). Furthermore, the use of these residues are regulated by council of regulation authorities, for establish the maximum residue limits (MRLs) for veterinary residues in foodstuff of animal origin (Koschorreck, Koch, & Rönnefahrt, 2002). The two primary processes of analyzing veterinary

residues were sample preparation and analytical procedures, all of which were fully explained (Wang et al., 2021). Sample preparations methods such as solid-phase extraction (SPE), liquid-liquid phase extraction (LLE) and matrix solid-phase dispersion (MSPD) are frequently used in the preparation of analyte samples before analysis (Beyene, 2016).

Solid phase extraction used for separation and purification of samples. It reduces the matrix interferences, enhance the sensitivity and identification of the target analyte. Moreover, SPE is time consuming and tedious techniques (Ares et al., 2017). Liquid-liquid extraction is a simple and rapid procedure for the analysis of these residues based on the different solubility and partition coefficient of the two compounds in two mutually incompatible (Zheng et al., 2014).

Matrix solid-phase dispersion is an efficient sample preparation method used for solid, semi-solid, liquid, and viscous samples. It is recognized as a one-step sample preparation technique for the extraction of various compounds from complex matrices (Tao et al., 2014).

Anthelmintics drugs are used to treat nematodes in both humans and animals. Furthermore, they work by targeting specific sites of action within the parasites neuromuscular system (Martin, 1997).

Triclabendazole (TCB) is a potent anthelmintic drug that has been widely used for the treatment of fascioliasis and is considered the drug of choice for this infection (Gandhi et al., 2019).

Triclabendazole acts as a selective inhibitor of tubulin polymerization, which is essential for the formation of microtubules in the parasite and subsequently disrupt the parasite cytoskeletal structure (Gandhi et al., 2019). The most common side effects of TCB include; decreased appetite, diarrhea, headache, increased sweating, skin rash, and stomach pain (Keiser, Engels, Büscher, & Utzinger, 2005). It is chemically represented as 6-chloro-5-(2,3-dichlorophenoxy)-2-(methylthio)-1H-benzimidazole (Sweetman, 2009) (Fig. 1).

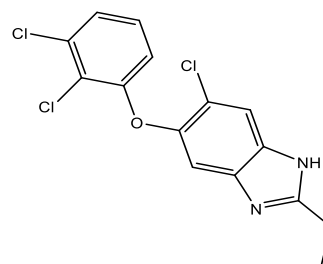


Fig. 1: 6-chloro-5-(2,3-dichlorophenoxy)-2-(methylthio)-1H-benzimidazole

To identify and quantify TCB in their pure form, pharmaceutical formulations, and biological matrices, a number of analytical techniques have been developed. An extensive overview of the analytical methods available for assessing TCB in different matrices are provided in this review paper.

2. Review on Analytical approaches

2.1. Spectroscopic methods

2.1.1. Spectrophotometric methods

Several spectrophotometric for determination of TCB in their bulk and pharmaceutical formulation. These reported methods are outline in **Table 1**.

Table 1: Spectrophotometric approaches for determination of TCB in different samples

Matrix	Type of determination	λ_{\max} (nm)	Ref
Bulk and pharmaceutical formulations	Indirect/depends on formation of colored complex product.	420 nm	(Ramadan, Mohamed, Shawky, & Salem, 2012)
Bulk and pharmaceuticals	Direct/ depends on measuring in <u>methanolic</u> 0.1M <u>HCl</u>	305 nm	(Shrivastava, Kumar, & Jain, 2011)
Pharmaceutical formulation	Indirect/ based upon redox reaction with Chloramine as oxidizing agent.	540 nm	(Rao, Sastry, Viplavaprasad, & Ramakrishna, 2014)

2.1.2. Spectrofluorimetric methods

One approach has been published for quantification of TCB in its pure and dosage form. It is represented in **Table 2**.

2.2. Chromatographic methods

Several chromatographic separation methods such as high-performance liquid chromatographic (HPLC), ultra-performance liquid chromatographic (UPLC) and thin layer chromatographic (TLC) have been developed and optimized for quantification of TCB in various matrices. These methods are summarized in **Table 3**.

Table 2: Spectrofluorimetric methods for determination of TCB in different matrices

Matrix	Condition	λ_{exi}	λ_{emi}	Ref
Pure and tablets	Depends on measuring its native fluorescence in methanol	298 nm	338 nm	(Belal, El-Din, El Enany, & Saad, 2014)

Table 3: Reported chromatographic methods for quantification of TCB in different samples.

Matrix	Stationary phase	Mobile phase	Detection	Ref
HPLC				
Pharmaceutical formulation	C18	Acetonitrile: methanol: water: acetic acid in ratio (56:36:7.5:0.5; v/v/v/v)	UV detection at 245 nm	(Shurbaji et al., 2010)
Bovin milk	C18	0.05 M ammonium acetate (pH 6): acetonitrile (50:50; v/v)	UV detection at 295 nm	(Takeba et al., 2000)
Milk	Stainless steel HSS t3 column (100mmx2.1 mm)	Gradient composition of acetonitrile: methanol with time programming	MS/MS	(Whelan et al., 2010)
Liver Flukes	C18	Gradient elution consisting of 0.025M ammonium acetate buffer (pH 6.5): acetonitrile with time programming.	UV detection at 300 nm	(Mottier, Moreno, Alvarez, Virkel, & Lanusse, 2004)
Pharmaceutical suspension dosage form	C18	Acetonitrile: methanol: water;(60:30:10; v/v/v)	UV detection at 254 nm	(Nischal, Somshekar, Abhilekha, Sharadamma, & Radhakrishna, 2011)
Water, honey, urine and plasma samples	C18	Methanol: water (80:20; v/v)	Fluorescence detection ($\lambda_{\text{emi}}/\lambda_{\text{exi}}$) 330/290 nm	(Asadi, Haji Shabani, & Dadfarnia, 2016)
Plasma and urine samples	C18	0.05M phosphate buffer (pH 7): acetonitrile (55:45; v/v)	UV detection at 312 nm	(Negro et al., 1992)
Milk sample	C18	Acetonitrile: water (60:40 ;v/v)	UV detection at 290 nm	(Zhou, Tai, Sun, & Pan, 2005)

Cont. Table 3: Reported chromatographic methods for quantification of TCB in different samples.

UPLC				
Bovin milk, muscle and liver	Stainless steel HSS T3 column with (100 mm x2.1 mm)	Gradient composition of trifluoroacetic acid: methanol (80:20; v/v) with time programming	MS/MS	(Whelan et al., 2013)
Sheep plasma	C18	Gradient elution of 0.1% formic acid in water and 0.1% formic acid in acetonitrile	MS/MS	(Farczádi, Dósa, Melles, & Vlase, 2021)
Livestock products	C18	Gradient elution of 0.1% formic :2 mM of ammonium format with time programming	MS/MS	(Park et al., 2023)
TLC				
Pure and pharmaceutical products	<u>Hypersil</u> BDS C18	Acetonitrile: 0.03M potassium dihydrogen <u>phosphate</u> buffer(70:30;v/v)	Densitometric detection at 215 nm	(Attia, El-Desouky, Abdelfatah, & Abdelshafi, 2023)

3- Conclusion

The current review covers an overview of several methods and procedures used in the quantification of TCB based on analytical data. Analytical chemists could obtain a significant insight from the review, enabling them to understand the basic solvents and the appropriate combinations of those solvents for the instruments employed in the analytical laboratory. Analytical chemists can gain knowledge about the benefits and drawbacks of different methods by examining comparative information provided in this scientific review.

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