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Literature Review on Spectrophotometric, Chromatographic and Voltammetric Analysis of Ivermectin

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Research Article

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Abstract

We will present the majority of the most recent published methods for determining the anti parasitic drug, Ivermectin in its pure form, combined form with other drugs, combined form with degradation products, and in biological samples in this literature review. This review also deals with the effectiveness of Ivermectin in treatment of COVID-19.

Keywords: Ivermectin; Degradation Products; Biological Samples; Literature Review; COVID-19

Introduction

Ivermectin (IVM) is an orally effective microfilaricidal agent that is a synthetic derivative of the antiparasitic family of compounds known as avermectin E. It is currently the most effective treatment for patients infected with the nematode Onchocerca volvulus, which is a leading cause of blindness in tropical areas. It's a macrolide endectocide that works on all endoparasites with cutaneous tropism (Strongyloides stercoralis, Ancylostoma braziliense, Cochliomyia hominivorax, Dermatobia hominis, Filaria bancrofti, Wucheria malayi, Onchocerca volvulus Loa-loa) and ectoparasites [1]. IVM is an antiparasitic drug with a wide range of activity, high effectiveness, and a high safety margin. This compound has been widely used in veterinary medicine since 1987, and its use in humans has been expanded [2]. IVM is supplied orally in a single dose of 150 mg/kg once a year. IVM is usually well tolerated, with the exception of a few extreme serious reactions such as significant systemic postural hypotension. When compared to diethylcarbamazine and suramin, which were commonly used to treat onchocerciasis, the medication has strong advantages in terms of ease of administration and tolerability. As a result, IVM is appropriate for use in mass-care programmes and is the most effective treatment choice for onchocerciasis currently available. As a result, it gives hope to tens of thousands of people who are on the verge of going blind, and it makes a significant contribution to tropical medicine [3]. The drug was developed as a result of a one-of-a-kind international partnership between the public and private sectors. In addition, the implementation process included the world's first and largest drug donation initiative, as well as a unique collaboration between governments, non-governmental organisations, and industry. The drug is now being used in two global disease-eradication programmes that support millions of the world's poorest people for free [4]. IVM activates unique IVM-sensitive ion channels in invertebrates, causing an influx of Cl-ions through the cell membrane. Muscle paralysis occurs as a result of the resulting hyper-polarization [5]. Due to the current importance of this drug in treatment of pandemic COVID-19, this literature focuses on its mode of action and different analytical methods that have been developed for determination of this drug in different pharmaceutical and biological samples.

IVM and Covid-19

Importin (IMP/1) binds to the coronavirus cargo protein in the cytoplasm (top) and translocates it into the nucleus

through the nuclear pore complex (NPC), where the complex disintegrates and the viral cargo reduces the host cell's antiviral response, allowing for increased infection. IVM binds to the IMP/1 heterodimer and nucleus. This leads to less inhibition of antiviral responses, resulting in a more natural and effective antiviral response [6].

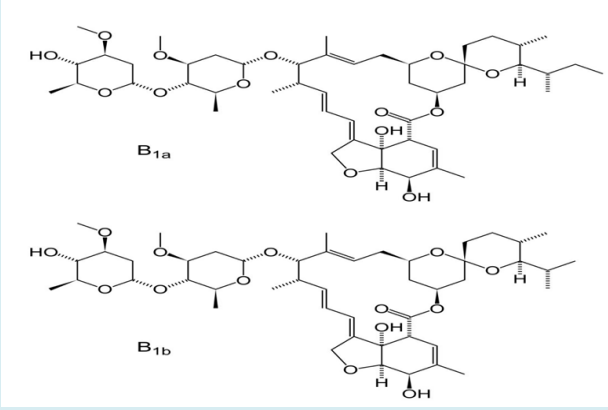

Figure 1: Chemical structure of IVM.

Review of Analytical Methods

Various techniques were used for the analysis of IVM in its pure form, combined forms, pharmaceutical formulations, and in biological fluids. The available reported methods in this literature can be summarized as follows:

Spectrophotometric Methods

LOD	Linearity range	λ_{max} (nm)	Method or Reagent	Matrix	Drug	Ref
---	5-40 µg/mL	314.4	UV Spectrophotometry	Tablet	IVM	[7]
---	10-200 µg/ mL	485	Visible spectrophotometry	Oral suspension and injection	Triclabendazole and IVM	[8]
µg/mL 0.029	5-15 µg/mL	245	Multivariate Spectrophotometry	Tablet	IVM	[9]
2.274 µg/mL	1.2-7.2 µg/mL	245	UV Spectrophotometry	Tablet	Levocetirizine and IVM	[10]
---	5-40 µg/mL	314.4	UV Spectrophotometry	Tablet	Albendazole and IVM	[11]

Chrmoatographic Methods

HPLC methods

Drugs	Matrix	Column	Mobile phase	Detector	Linearity range	LOD	Ref
IVM	Meat and liver	µ- Bondapak C_{18}	Acetonitnie and water	fluorescence detection	---	250 pg	[12]
IVM, FEBANTEL, PRAZIQUANTEL, PYRANTEL PAMOATE	Tablets	C_8 column (50 x 2.1 mm i.d) coupled with a C8 (10 x 2.1 mm i.d) guard column	Water/acetonitrile (15:85 v/v) containing 0.1% formic acid and 3 mmol/L ammonium formate	MS/MS	40-200 ng/mL	0.5 ng/ mL	[13]

IVM	Liver	Bond-Elut C_8 column	Methanol:water (96:4 v/v)	fluorescence detection	2.48 - 24.8 ng per g tissue	1 ng per g tissue	[14]
IVM	Human plasma	Hypersil Gold C_{18} column (150 x 4.6 mm, 5 microm particle size)	Acetonitrile, methanol and distilled water (50:45:5, v/v/v)	Fluorescence detection	3-13600 µg/L	1 µg/L	[15]
triclabendazole and IVM	Pharmaceutical Formulation	C_{18} RP column	Acetonitrilemethanol wateracetic acid (56 36 7.5 0.5, v/v/v/v)	UV at 245 nm	27.01-81.02 µg /mL	0.07 µg / mL	[16]
IVM	Reindeer feces	C_{18} solid-phase extraction column	Acetone, isooctane	Fluorescence detection	5–2000 ng/g wet weight feces.	---	[17]
clorsulon, albendazole, triclabendazole and IVM	Pharmaceutical preparations	Monolithic column	120 mM sodium dodecyl sulfate, 15% propanol and 15 mM phosphate buffer (pH 5.5)	UV at 225 nm	30–300 µg/ mL	6.15 µg/ mL	[18]
IVM	Milk	SPE C_{18} column and SPE silica column	Acetonitrile, water and triethylamine	Fluorescence detection	2.8-55.6 ng/ mL	0.5 ng/ mL	[19]
IVM	Animal tissues	SPE C_{18} columns	95:5 v/v methanol:water	Fluorescence detection	10-120 ng/g	2 ng/g	[20]
IVM	Pig serum	Phenomenex C_{18} (5 microm, 250 mm x 4.6 mm)	Methanol and water in the ratio of 90:10 (V/V)	Fluorescence detection	0.010-20 mg/L	0.010 mg/L	[21]
IVM	Plasma	Supelcosil LC-18 column	Acetonitrile and water (96:4, v/v)	UV detection	1 - 40 µg/L	0.5 µg/L	[22]
IVM	Plasma	RP column (C_{18}, 250 × 4.6 mm, 5 µm) with a security guard column (C_{18}, 10 × 4 mm, 5 µm) (Phenomenex, Torrance, CA)	Methanol and water (90:10)	UV detection	20–1000 ng/ mL	---	[23]
IVM	Cattle and Sheep Tissues	Du Pont Zorbax ODS (4.6 mm X 15 cm	Methanol-water (95:5)	UV detection	---	1-2 ppb	[24]
IVM	Animal liver : cattle, goats, sheep and swine	SPE C_8 and silica gel columns	Methanol–water (98 : 2)	Fluorescence detection	7.5–30 ng/g	2.5 ng/g	[25]
IVM and moxidecin	Bovine milk	Selectosil C_{18} (5 mm, 250 £ 4.60 mm) reverse-phase column	Acetic acid (0.2% in water), methanol and acetonitrile (4:40:56 v/v/v)	Fluorescence detection	0.1-50 ng/mL	0.033 ng /mL	[26]
IVM	Meat samples	RAMIP-BSA column	methanol:water (70:30, v:v)	UV detection	50-500 µg/ kg	16.66 µg/ kg	[27]

abamectin (ABA), emamectin (EMA) benzoate and IVM (IVM)	Rice	Waters Xbridge C_{18} column (250 4.6 mm i.d., 5 mm) with a guard column (20 4.6 mm i.d., 5 mm)	Acetonitrile/ methanol/ water (10 : 80 : 10, v/v/v)	Fluorescence detection	0.01 - 5 µg/mL	1.3 µg/ kg	[28]

HPLC methods

Drug	Matrix	Stationary phase	Mobile phase	Detector	Linearity range	LOD	Ref
IVM	Tablets	Lichrospher TLC aluminum plates pre-coated with silica gel 60F-254 (20cm×10cm×200 :m)	n-hexane: acetone: ethylacetate (6.5: 3.5: 0.1 v/v/v)	UV at 247 nm	100-5000 ng/spot	8.22ng/ spot	[29]
IVM and Albendazole	Tablets	aluminum-backed silica gel 60 F254 layers	toluene-ethyl acetateglacial acetic acid, 6:4:0.5 (v/v/v))	UV at 247 nm	0.12 - .54 µg/band	0.02 µg/ band	[30]
Closantel and IVM	Vials	Silica gel 60 F254 plate	Toluene: isopropanol: ammonia 33%: 11 glacial acetic acid (70:28:10:1, by volume)	UV at 245 nm	0.06-3 µg/ band	0.013 µg/band	[31]

Voltammetric Methods

Drug	matrix	electrode	linearity	LOD	Ref
IVM and levamisolein anthelmintic and urine samples	Pharmaceutical formulations and urine	Cathodically pretreated boron-doped diamond electrode	0.60–50 µmol/L	0.30 µmol/L	[32]
IVM	Urine and tape water	Silver nanoparticles (AgNPs) modified boron and sulfur co-doped reduced graphene oxide (B, S@rGO)	0.3-60.0 nM	0.1 nM	[33]

Conclusion

This literature review represents an up to date survey about all reported methods that have been developed for determination of Ivermectin in its pure form, combined form with other drugs, combined form with degradation products, and in biological samples such as spectrophotometry, liquid chromatography, voltammetry, etc.

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