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Review Article

A Mini Review On the Analytical Methods for Individual and Drug Combinations Administered in Mass Drug Administration for Lymphatic Filariasis

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Abstract: The NTDs (Neglected Tropical Diseases) are the group of diseases considered the diseases of the poor. Lymphatic Filariae (LF) is one of the category that is prevalent mostly in 47 countries and around 863 million people are under threat from this category of disease. A program named Global Programme to Eliminate Lymphatic Filariasis (GPELF) was initiated by WHO (World Health Organisation) in 1998, with the aim of eliminating LF by 2020. The main role of GPELF was to initiate measures to stop the spread of disease and to control the suffering caused by disease to the patients. For controlling the spread of disease, mass drug administration (MDA) was initiated where the drug or their combinations were administered annually or as and when required. This initiative was Alternating Mass Drug Administration Regimens to Eliminate Lymphatic Filariasis. The recommendations depended on the causative organism and co-endemicity of LF with other filarial diseases. The drug recommendations by WHO for MDA were; for areas with LF and loiasis, albendazole in a dose of 400 mg twice a year; for areas with onchocerciasis and LF, ivermectin in a dose of 200 mcg/kg along with albendazole 400 mg; for areas without onchocerciasis diethylcarbamazine citrate (DEC) in a dose of 6 mg/kg combined with albendazole in dose 400 mg. The three-drug combination was also recommended in some cases where onchocerciasis was not prevalent with LF. Many clinical trials also started for comparing one, two, and even three-drug combinations. A document to streamline the use of these drugs for LF was also issued by WHO in 2017 with the name Alternating mass drug administration regimens to eliminate lymphatic filariasis. The achievement with these regimens, till 2020 was that 80 percent of countries endemic to LF have achieved elimination of this disease. Further, to achieve better elimination in other countries a road map for 2020-2030 is now in being. The analytical methods for individual drugs as they are very old drugs were available and some of the methods for combination are also there mostly involving High-Performance Liquid Chromatography (HPLC) with different types of detecting combinations. These methods are given for detection in various clinical trials or used as an analytical method for the determination of drug(s) in dosage forms.

Keywords: Lymphatic Filariasis, Mass Drug Administration, Albendazole, Diethylcarbamazine Citrate, Lymphedema, Elephantiasis, Ivermectin.

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1. INTRODUCTION

Over 947 million individuals worldwide are at risk of contracting lymphatic filariasis (LF)[1], and an estimated 67.88 million are infected, with up to 36 million deformed and handicapped as a consequence of the disease's chronic complications[2]. According to the World Health Organization (WHO), LF is responsible for at least 2.8 million disability-adjusted life years (DALYs), excluding the considerable co-morbidity of mental illness typically encountered by patients and carers[1,3]. This illness affects the lowest members of society, notably those living in places with inadequate water, sanitation, and housing, resulting in lifelong disfigurement, decreased productivity, and social stigma[4]. The most prevalent chronic symptoms of LF are elephantiasis (limb swelling), lymphedema (skin swelling), as well as hydrocele (swelling of the genital organs)[5]. The disease lymphatic filariasis (well-known as elephantiasis), is a disease under the category of NTDs. Lymphatic filariasis is a parasitic infection that affects mostly the lymphatic system and can cause abnormal enlargement of body parts mostly legs but other parts arms, breasts and genitalia can also be affected, resulting in pain, severe disability, and social stigma. This is the group of infections caused by nematodes (worms) belonging to the family Filarioidea, commonly known as lymphatic dwelling *filariae*. The organisms most commonly causing the disease are *Wuchereria banocrofti* (90%), *Burgia malayi,* and *Burgia timori*[6]. The two co-infections with this disease are, eyeworm *(Loa loa*) and river blindness *(Onchocerca volvulus)*. Table 1 gives the detail of the vector for different organisms.

Table 1. Lymphatic filariasis causative organisms and their vectors

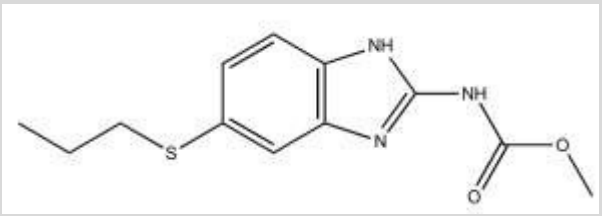
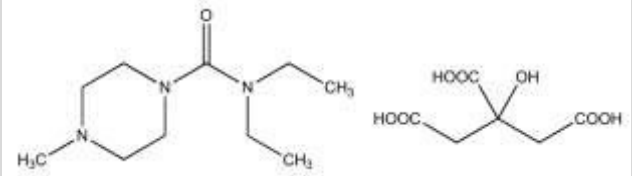
Causative organism(1)	Vector
Wuchereria banocrofti	Mosquito genus Anopheles - Acdes, Culex, Mansonia, Coquillettidia
Burgia malayi	Mosquito genus Mansonia, Aedes
Burgia timori	Midge (genus Culicoides)
Loa loa	Fly (genus Chrysops)
Onchocerca volvulus	Black fly

It is to be noted that all of these have a vector component which is a necessity for the spread of the disease. The major concern is disabilities associated with this category of disease which includes acute lymphangitis, filarial abscess, elephantiasis, hydrocele, tropical pulmonary eosinophilia, and lymphadenopathy. WHO established the "Global Programme to Eliminate Lymphatic Filariasis (GPELF)," with the main goal of the initiative is disease control and elimination by 2020. [7, 8].Eradication of Lymphatic filariasis can be achieved by controlling the spread of infection through yearly preventive chemotherapy with some safe medicine combinations. The initiative was aided further by mass drug administration started from 2000. Since 2000, more than 8.6 billion treatments have been administered to control the spread of infection. The data on mass drug administration was not systematic until 2016, so uniform regimen guidelines were published in 2017 by WHO.[8] In 2018, there was a decrease of 74 percent (51 million people) infections since 2000, when WHO's GPELF started. The initiatives including preventive chemotherapy have a great achievement wherein 692 million people are there who are no longer dependent on preventive chemotherapy.[8] In 2020, GPELF set new goals for the NTD as road map 2021-2030. According, to it 58 (80 percent) of endemic countries have met the criteria for validation of LF elimination as a public health problem, with both sustained infection rates below target thresholds for at least 4 years after stopping MDA and providing the essential package of care in all areas with known patients; 72 (100 percent) of endemic countries implement post-MDA or post-validation surveillance, and reduction to 90 % of patients requiring interventions[9].

1.1 Drugs and their combinations recommended for Lymphatic filariasis

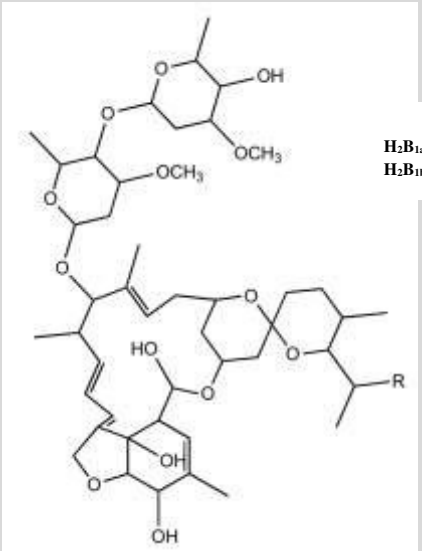
The preventive chemotherapeutic agents recommended for the control of the disease are listed in Table 2. The table also contains structure and the detail of the physicochemical properties of the drugs.

Table 2: Chemical names, structures and physicochemical properties of selected drugs[5]

Drug /IUPAC name Structure	Intrinsic Solubility (mg/ml) #	pKa	Log P*	UV λ_{max} nm
Albendazole  **Methyl [5-(propylsulphanyl)-1H-benzimidazol-2-yl] carbamate**	0.01	9.51 4.27	2.55	254 295
Diethylcarbamazine citrate 	0.06	6.9	0.09	204

N, N-diethyl-4-methylpiperazine-1-carboxamide

Ivermectin



R
H_2B_{1a} -CH_2CH_3
H_2B_{1b} -CH_3

238

5.83

12.47

-3.4

(1R,4S,5'S,6R,6'R,8R,10E,12S,13S,14E,16E,20R,21R,4S)-6'-[(2S)-butan-2-yl]-21,24-dihydroxy-12 [(2R,4S,5S,6S)-5-[(2S,4S,5S, 6S) -5-hydroxy-4-methoxy 6-methyloxan-2-yl] oxy-4-methoxy-6-methyloxan-2-yl]oxy-5',11,13,22-tetramethylspiro[3,7,19-trioxatetracyclo [15.6.1.14,8.020,24] pentacosa-10,14,16,22-tetraene-6,2'-oxane]-2-one

The dose and the drug combinations recommended by various guidelines and based on the clinical trials conducted for these combinations are listed in Table 3.

Table 3: Disease state and mass drug administration recommended[8]

Disease state	Recommendations	Dose
Lymphatic filariasis (LF)	Annual DA / IDA (some cases)	I – 150–200 µg/kg D – 200 mcg/kg A - 400 mg
LF co endemic with Onchocerciasis	Annual IA	I – 150–200 µg/kg A - 400 mg
LF is co-endemic with loiasis and / or Onchocerciasis	Biannual albendazole	400 mg

LF- lymphatic filariasis, DA - diethylcarbamazine + albendazole, IDA - ivermectin + diethylcarbamazine + albendazole, IA - ivermectin + albendazole.

A three-drug regimen comprising ivermectin, diethylcarbamazine (DA) and Albendazole (IDA) was introduced by the WHO as an alternative MDA regimen to accelerate the LF elimination program[8]. MDA helps in primary prevention by lowering and reducing transmission rates among at-risk populations. Furthermore, MDA can prevent the progression of subclinical to clinical disease and deteriorating morbidity, contributing to economic savings at the community level. The effectiveness of MDA in reducing the prevalence and density of microfilaria in the blood is directly related to the proportion of the population who consume the drugs annually

1.2 Albendazole

Albendazole (ALB), an benzimidazole anthelmintic (methyl 5-propylthio-1H- benzimidazol-2-yl-carbamate) with broad-spectrum of activity and is used for the treatment of intestinal helminthic infections caused by a nematode (*Necator americanus*, *Ancylostoma duodenale*, *Ascaris lumbericoides*, *Trichuris trichiura*, *Trichinella spiralis*, *Loa loa*, *Onchocerca volvulus*) and cestode (*Taenia saginata*, *Taenia solium*). The drug is effective in mixed infections also. This drug is one of the drugs in WHO List of Essential drugs.[6]

Mechanism of action

1.3 The main mechanism of albendazole activity are as follows-

1) Albendazole can cause progressive alterations in the worm's intestinal cells by combining specifically to the tubulin's colchicine-sensitive location, hence preventing their polymerization to form microtubules.

2) This causes impairment in the uptake of glucose by the susceptible parasites (the larval as well as the adult stage) thus, diminishing the stores of glycogen. These changes which are degenerative are triggered in the ER (endoplasmic reticulum), the geminal layer, mitochondria, and cause decreased production of adenosine triphosphate (ATP) because of the release of lysosomes[10]. ATP is important for the life of the helminth. This causes immobilization of the parasite and ultimately their death.

3) Albendazole is very less soluble and has wetting problems also, so its absorption from the GIT (gastrointestinal tract) is low. A fatty diet can enhance its oral bioavailability.

1.4 Some of the Reported analytical methods for Albendazole[11-13]

To date, many studies exist on the development of SIAMs (Stability Indicating Analytical Methods) for ALB that reveals the photolytic, hydrolytic along with oxidative effects on the drug, but no work was conducted for the structure elucidation of any of its degradation products. Several LC and LC-MS methods have been reported for analysis of ALB in different matrices, including dosage form, blood, and urine. Some of the reported methods are enlisted in Table 4.

Table 4. Reported analytical methods in literature for Albendazole

Applications	Column	Mobile phase	Detector	Reference
Method for determination of diethylcarbamazine, doxycycline and metabolites of albendazole in single run	C18 HPLC column (Xselect CSH) Waters dimensions 3.0 mmx 150 mm, particle size 3.5 µ m	Elution was gradient and mobile phase consisted of 0.1% formic acid solution in water : methanol	Mass spectrometry	14
Quantification of Albendazole metabolites in plasma	C18 column dimensions 250 mm length and 4.6 mm diameter, particle of 5µ m size	Mobile phase was Acetonitrile with 0.025M ammonium phosphate buffer having pH - 5, flow of mobile phase- 1.2 mL/min	295 nm	15
Chromatographic determination by using of Crossed D-Optimal design for anthelmintic	C18 column was used having dimensions 250 mm × 4.6 mm having particle 5 µ m size at 40 °C	Mobile phases used 1) combination of methanol, water with acetonitrile 2) 0.05M ammonium acetate buffer having pH 5.5: acetonitrile : methanol (40:37:23) mobile phase pumped at a flow rate of 1 mL/min	Ultraviolet diode array detector	16
Biotransformation by fungus of albendazole	Column used- Chiralpak AS .	Mobile phase-acetonitrile to ethanol (97:3) and 0.2% triethylamine with 0.2% acetic acid flow of mobile phase 0.5 mL/min	290 nm	17
Kenya market evaluation of albendazole in deworming formulations	Stationary phase used is VP – ODS	Mobile phase - Monobasic sodium phosphate-11.0 g dissolved in 800 ml water and adding 1200 ml methanol	288nm	18
HPLC determination of albendazole soft capsules and its related substances	YMC-Pack ODS-A column having dimensions 6.0 × 150 mm with particle size 5 µ m	mobile phase consisted of 0.125%, N(98)H4H2PO4 (65:35). The flow rate was 1.0 mL/min	254 nm	19

Estimation of albendazole and its metabolites in serum of humans	Column used was C8-RP	Mobile phase - acetic acid: methanol: water: acetonitrile-10:40: 49:1	286 nm UV and Fluorescent measurement	20
Clinical Pharmacokinetic method for albendazole and its metabolites	Column- µ Bondapak Ph (Waters) dimensions 3.9 mm×300 mm	Mobile phase used triethylamine (1.25%) in water (pH 3.1): acetonitrile :methanol- 72:13:15, Flow of 1.0 mL/min	295 nm	21
Determination of albendazole in tablet dosage form	C-18-RP column	Acetonitrile and H_2O with triethylamine 0.4% having pH 3.6 and having ratio of 46: 54	254 nm	22
Method of determining albendazole in dosage form	C18 RP column - Lichrosorp 10	Tetrahydrofuran and water in ratio 55:45 and adding 0.5% acetic acid to it	296 nm	23

So far, no methodical study on the stress degradation behavior of ALB under forced conditions as prescribed by ICH and WHO are reported. The analytical methods described for albendazole are mostly using C18 columns and using methanol and/or acetonitrile with buffer to maintain the pH. The detection methods used are UV, PDA(photodiode array), and MS.

1.5 Diethylcarbamazine citrate

Diethylcarbamazine citrate (DEC), a piperazine derivative that is generally recommended for the treatment of filariasis when existing along with onchocerciasis or loiasis. Though it is inactive in vitro, it shows activity in vivo and has a very rapid onset of action. The major side effect of the drug is a fatal anaphylactic reaction (Mazzotti reaction), caused when the adult filarial count is high.[6]

1.6 Mechanism of action

The three mechanisms are suggested for the action of DEC-1) This mechanism involves triggering the blood platelets to the presence of filarial excretory antigens. The drug may cause morphological damage to the microfilaria. The damage is done to the cellular sheath, exposing antigen to immune mechanisms, leading to damage to organs and ultimately death.

2) The second mechanism is similar to albendazole which involves inhibition of microtubule polymerization along with disruption of tubules which are performed.

3) The third mechanism is interference in the arachidonic acid pathway at the cyclooxygenase and leukotriene A_4 synthetase levels. This influences cellular adhesiveness and activation of cells.

1.7 Indications

The drug is not most effective against adult worms; therefore, it is mostly used in combination with ALB or ALB and IVR in the treatment of lymphatic filariasis when with the co-existence of *Loa loa, Onchocerca volvulus* (three-drug combination), and along with IVR in *Wuchereria bancrofti* and *Brugia malayi*.[8]

1.8 Some of the Reported analytical methods for Diethylcarbamazine

A number of HPLC methods have also been reported for the assay of the drug using UV as well as MS detectors. Some of them are enlisted in Table 5 along with chromatographic conditions.

Table 5. Reported analytical methods in literature for Diethylcarbamazine

Applications	Column	Mobile phase	Detector	Reference
HPLC method for diethylcarbamazine and levocetirizine combination in Tablet dosage form	Princeton Sphere-100 C18 (250×4.6 mm. 5 µ) column	20 mM KH_2PO_4 (potassium dihydrogen orthophosphate) buffer pH 3.2 Buffer : acetonitrile 50:50 v/v, Flow isocratic Flow rate 1.0 ml/min	UV detection-224 nm wavelength	24

Combination of Chlorpheniramine maleate and diethylcarbamazine citrate in pharmaceutical dosage forms	Kromasil C^{1}_{8} column (25^{0}mm, 4.6 mm, 5mm)	Acetonitrile:$^{0.01}$M KH_2PO_4 buffer adjusted to pH $3.^{0}$ with ratio 8^{0}:2^{0}, flow rate was $^{1}.^{0}$ ml/min	UV detection 238 nm	[25]
Analysis of diethylcarbamazine citrate in medicated salt by HPLC	Luna C8 column (Phenomenex) dimensions $^{1}5^{0}$ mm ×4.6 mm dia.	Buffer 2^{0} mM KH_2PO_4 buffer (pH 3.2) Buffer: Acetonitrile 9:^{1} Flow rate $^{0}.5^{0}$ ml/min	UV wavelength 2^{10} nm	[26]
Determination of diethylcarbamazine citrate along with chlorpheniramine maleate when in dosage form	Sunfre C^{1}_{8} column, 25 cm in length and 4.6 mm i.d	pH of 5.5 for mobile phase, ratio of mobile phase is ^{10}:9^{0}:$^{0.1}$ for water:methanol:^{10}% triethylamine, flow rate $^{1}.^{0}$ mL/min.	UV detection 225 nm	[27]
LC-MS analysis for diethylcarbamazine for in human plasma useful in clinical pharmacokinetic studies	Phenomenex synergi fusion-rp (2 mm × 25^{0} mm)	Mobile phase $^{0.0}$5% formic : acetonitrile 46: 64% Flow rate ^{0}.25 mL/min.	Mass spectrometry	[14]

A comprehensive LC and LC-MS study of the degradation behavior under various ICH prescribed stress conditions has been lacking for this drug even.

1.9 Ivermectin

Ivermectin, a mixture of 22, 23-dihydro-avermectin B^{1}_{a} and B^{1}_{b} in the ratio of 9^{0}:^{10} (approx.) [13,14]

1.10 Indication

Ivermectin is a semisynthetic avermectin and also a macrocyclic lactone having a disaccharide. It is derived from *Streptomyces avermitilis*, a bacterium found mostly in the soil. The category is very potent and is used mainly for the treatment of nematode infections mainly caused by *Enterobius vermicularis*, *Ascaris lumbricoides*, *Trichuris trichura*, *Wuchereria bancrofti*, *Loa loa*, *Onchocerca volvulus*, *Burgia malayi*[6,28].

1.11 Mechanism of action

The binding increases as the permeability for chloride ion of the cell membrane increase thus, resulting in hyperpolarization of the cells. This leads to paralysis and finally leads to the parasites' death. The drug has high affinity to these channels. It may also act on gamma-aminobutyric acid (a neurotransmitter) agonist causing disruption of neurosynaptic transmission controlled by GABA in the central nervous system (CNS). The drug can weaken the normal development of *O. volvulus* microfilariae in the uterus and thus leading to a reduction in the release of them the female worms.

1.12 Some of the Reported analytical methods for Ivermectin

There are multiple reports on HPLC methods for the analysis of the drug in different matrices using UV, fluorescence, and MS detectors (Table 6).

Table 6. *Reported analytical methods in literature for Ivermectin*

Applications	Column	Mobile phase	Detector	References
UPLC and HPLC-FD method for	C8 Acclaim™ $^{1}2^{0}$ column having dimensions 25^{0} mm and 4.6 mm particle with size of 5 µm	Isocratic elution of mobile phase consisting of acetonitrile : methanol: Tetrahydrofuran in ration 96:^{1}:3 pumped isocratically with a flow of ^{0}.8 mL/ min	- Fluorescence detection MS/MS	[29]

determining avermectin				
Simultaneous estimation of ivermectin, praziquantel and pyrantel	Column C8 with dimensions 5^{0}mm × 2.^{1} mm internal diameter	Mobile phase composing of acetonitrile: water in ratio ^{1}5:85 having formic acid ($^{0.1}$%) and ammonium formate (3 mmol/L) in isocratic elution having flow rate-2^{00} µ L/min	Mass Spectrometry	[30]
Determination of emamectin B^{1}a, abamectin B^{1}a and ivermectin in soil samples	SPE (solid phase extraction) on C^{1}8	Water: acetonitrile in ration ^{1}:9	Fluorescence detection	[31]
Estimation of ivermectin and avermectin in beef tendon	C^{1}8 chromatographic column with dimensions 4.6 mm and ^{1}5^{0} mm, 5 µ m particles in stationary phase	Mobile phase consists of water and acetonitrile having ratio of 3:97	Detection by fluorescence	[32]

However, there is no comprehensive report on the degradation chemistry of the drug.

1.13 Combination of drugs

The combination of drugs[33] is generally recommended to achieve an improvement in efficacy, reducing toxicity (as doses adjustment needed) and further an important aspect reduction in resistance to a single drug. The drugs used for study are from different classes thus having a different mechanism of action as already discussed earlier.

1.14 Albendazole and Diethylcarbamazine [34,35]

The drugs for treatment and dosage regimen for the NTD category of diseases were not systemized and many different regimens were followed. So, World Health Organization (WHO) 2017 issued, the "*Guideline for Alternative Mass Drug Administration Regimen to Eliminate Lymphatic Filariasis*"[8]. According to the guidelines, the drug combination of albendazole and diethylcarbamazine is one of the recommendations for filariasis when it is not co-endemic with eye infections. The methods for combination of both the drugs are shown in Table 7.

Table 7. ***Reported analytical methods for combination of albendazole and diethylcarbamazine***

Applications	Column	Mobile phase	Detector	References
Method for estimation of metabolites of albendazole, diethylcarbamazine and doxycycline	C18 Xselect CSH™ column having dimensions 3.0mm x 150 mm and particle having size of 3.5 µ m	Elution is gradient and Mobile phase-formic acid (0.1%) in water with methanol	MS detection	36
Analytical method for combination of albendazole and diethylcarbamazine along with metabolite of albendazole in plasma	UPLC (C18) Acquity having BEH column, dimensions are 100 × 2.1 mm particles 1.7 µ m in size	Elution gradient formic acid (0.05%) in methanol as mobile phase	MS/MS	37
Estimation of albendazole, its metabolites and diethylcarbamazine rat plasma	C18 Xselect Column dimensions 3.0 mm x150 mm, Particle size of 3.5 micrometre	Methanol and formic acid (0.1%) in water	MS detection	38

1.15 Albendazole and Ivermectin

This combination is recommended where in any part of country if onchocerciasis is endemic and if lymphatic filariasis prevalent with either loiasis or onchocerciasis. Table 8 represents methods for combination of albendazole and ivermectin

Table 8. Reported analytical methods for combination of albendazole and ivermectin

Applications	Column	Mobile phase	Detector	References
Anthelmintic drug residues in beef	C18 UPLC Acquity HSS T3 columns dimensions 100mm X2.1 mm	Phase 1 -water :0.01% acetic acid in acetonitrile: (90:10, v/v) phase 2 - acetonitrile: ammonium formate (5 mM) ratio of 25:75	MS detection	39
Determine veterinary drug in waste sludge	C18 column Acquity BEH dimensions 50 ×2.1 mm and particle size 1.7 µ m	solvent A (0.1% formic acid) and solvent B acetonitrile :methanol in ratio 80:20, at a pumped at 0.4 mL/min	Tandem mass	40
Veterinary drugs residues in bovine muscle	Agilent C-18 Zorbax Eclipse XDB column with dimensions of 150mm × 4.6 mm and particles of 5 µ m size	a mobile phase consisting Ammonium acetate (10mM) in water (A) and formic acid (0.1%) in methanol (B).	MS	41
Determination triclabendazole and ivermectin in formulation	RP C18 column	Mobile phase of methanol: acetonitrile: acetic acid :water in the ratio 36 : 56 : 0.5 : 7.5, pH of mobile phase 4.35 its pumped at 1.0 mL/min	245 nm	42
Determination of Ivermectin and albendazole in tablet dosage form	C18 RP column NUCLEODUR with dimensions 250 mm× 4.6 mm, 5 µ	Mobile phase methanol: acetonitrile: water in ratio of 30:60:10 flow of 1.8 mL/min.	245 nm	43

For the estimation of ivermectin alone or concurrently with its metabolites in biological fluids/formulations, analytical methods such as liquid chromatography[37–40], liquid chromatography, capillary electrophoresis, immunoaffinity column cleanup procedure[41], combined with positive electro spray ionisation tandem mass spectrometry (ESI-MS/LC/MS), and biosensor immunoassay based on surface plasmon resonance[42] have been reported. However, there hasn't been any information published on a spectro-photometric technique for estimating combined albendazole and ivermectin in tablet dose form.

1.16 Albendazole, Diethylcarbamazine and Ivermectin

The combination is recommended as superior to other regimens available and is also effective in onchocerciasis. The combination also causes more effective clearance of microfilariae in patients. The combination has a far more

superior killing effect on the parasites. The literature data on the analytical methods for three-drug combinations is not available.

1.17 Side Effects related to MDA

The most frequent adverse reactions associated with the administration of MDA are dizziness, nausea, fever, malaise, headache, vomiting and reduced appetite.[24] However, incorporating information about side effects throughout the overall health awareness program while highlighting the fact that they were temporary and therefore not clinically dangerous was another crucial aspect of controlling these negative effects.

2. DISCUSSION

We are currently in an exciting period when MDA associated with specific NTDs already has significantly improved world health, especially among the poor, by avoiding or reducing morbidity. Studies on the pharmacokinetics of the single-dose, two-regimen medications have demonstrated that all three medications, whether taken alone or in combination, were safe for both microfilaremia and non-microfilaremia people and were well tolerated by the body.[14,15] Research to ascertain the effectiveness of these medications revealed that a combination of ALB + DEC, ALB + IVM, and DEC + IVM caused large drops in mf levels over extended periods when given in repeated yearly MDAs.[26] Outside of places where onchocerciasis and loiasis are prevalent, it was also determined that the combination of DEC + IVM is safe to use.[27] Testing the two-drug vs one-drug regimen revealed that the inclusion of ALB consistently reduced or completely eliminated mf in those who were impacted. It has been established by six microsimulation models that MDA has an impact on LF eradication. The significance of relevant and timely community - based health education programmes in MDAs for LF have already been recognised by several other research.[37-39] The distribution, demography, and ecology of various NTDs, as well as the benefits and drawbacks of current management measures, must all be carefully taken into account for integration to be successful. When preparing MDA for LF, several experts have indicated that it's essential to keep an eye on population trends.[32] However, on its own, MDA probably won't be enough in the long run. There is a need for new or improved medications or vaccinations, as well as more funding for studies into the fundamental biology, capacity for evolution, as well as dynamics of disease transmission. A focus on enhancing the MDA strategy's effectiveness is required. To do this, better monitoring and evaluation (M&E) techniques must be developed, especially those that address any decline in drug efficacy or emergence of resistance. Health education programmes that are tailored to local cultural and social contexts will be necessary for strategies to ensure consistent high inclusion over many years.

3. CONCLUSION

The development of a single HPLC method for the combination of any two- or three-drug out of ALB, DEC, and IVR require that the individual drug should elute at different times i.e., one in starting, second in the middle, and third in the end part. The three drugs have different solubilities profiles this will require an optimized method for preparing the sample of each drug individually and in combination with varying combinations of solvents. The other important aspect is the careful selection of the absorption region of the ultraviolet region as all the drugs absorb at different wavelengths, whether it is possible to detect two drugs at the same wavelength or to use a single wavelength. The other part is the development of a method for elution where modification in the organic phase (type and its ratio), aqueous phase – whether to use buffer, its type, concentration, and pH selected to be optimized. Further, to reduce the likelihood of transmission of the LF infection, it is essential to recognize the context-specific aspects that affect how MDA for LF is implemented. If we are to achieve the goal of eliminating the disease, this understanding will serve as the foundation for all planning, organisation, and execution of MDA for LF. Consequently, it is advised that studies on MDA for LF concentrate more on the highlighted key implementation challenges rather than only medication administration and uptake. By using some of the common procedures used in implementing research models, further studies should examine in depth the various methods utilised to enhance MDA for LF implementation.

4. AUTHOR CONTRIBUTION

Dr. Mohini Kalra conceptualized and designed the concept of the study and Dr. (Mrs.) Sanju Nanda curated the data and provided the necessary points to be modified. The data was corrected accordingly and compilation of the manuscript.

5. CONFLICT OF INTEREST

Conflict of interest declared none.

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