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List of Abbreviations

ABZ	Albendazole
AR	Anthelmintic Resistance
ATP	Adenosine Triphosphate
AVM	Avermectins
BP	British Pharmacopeia
bw	Body weight
BZs	Benzimidazoles
DD	Discrimination/delineating dose
EHDDT	Egg hatch discrimination dose test
EPG	Egg per gram
FEC	Faecal Egg Count
FECR	Faecal Egg Count Reduction
FECRT	Faecal Egg Count Reduction Test
GIT	Gastrointestinal Tract
GIN	Gastrointestinal Nematode
GOT	Glutamic Oxaloacetic Transaminase
GSP	Good Storage Practice
HPLC	High Performance Liquid Chromatography
IVM	Ivermectin
LDA	Larval development assay
LEV	Levamisole
LMIA	Larval migration inhibition assay
MDR	Multiple Drug Resistance
MDH	Malate dehydrogenase
mg	Milligram
gm	Gram

mL	Millilitre
MLB	Milbemycins
MLs	Macrocyclic Lactones
MMT	Micro- motility meter test
rpm	Round per minute
W.A.A.V.P.	World Association for the Advancement of Veterinary Parasitology
NADH	Nicotinamide Adenine Dinucleotide Hydride
NADPH	Nicotinamide Adenine Dinucleotide Phosphate Hydride
nAChR	Nicotinic acetylcholine receptors
NMJ	Neuromuscular junction
NMPB	National Medicines and Poisons Board
LDA	Larval development assay
TET	Tetramizole
v/v/v	Volume/ Volume/ Volume
v/v/w/v	Volume/ Volume/ Weight/ Volume
w/v	Weight/ Volume
µg	Microgram

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Abstract

Following several reports indicating reduced efficacy of some anthelmintics in sheep in different parts of the Sudan; faecal egg count reduction test was used to report on therapeutic efficacy of four anthelmintics common in use in sheep health care procedures in the field. In the current study, 16 male sheep with confirmed gastrointestinal nematodes (GINs) infection were used to evaluate the efficacy of Albendazole 2.5% drench formulation and to compare obtained results with that of Ivermectin 0.8% drench formulation. Samples of the drugs (the same batch) were randomly selected and tested before the start of the experiment to ensure satisfaction of finished product specification. Animals were divided into two groups each of eight animals; sheep in the first group (A) were drenched orally with albendazole at 5mg/kg body weight (bwt) as single dose, while animals in the second group (B) received ivermectin oral solution at dose rate of 0.2mg/kg bwt. Faecal samples were collected at the following intervals: 0 (before treatment), and then at 2, 3, 4, 7, 10, 14, and 21 days (post treatment). Blood samples were collected from sheep before and following treatment to evaluate the effect of treatment on some blood metabolites namely: total proteins, albumin, urea, aspartate aminotransferases, alanine aminotransferases, calcium and phosphorus. Results obtained indicated that there is no evidence of efficacy in the two treatment groups (albendazole and Ivermectin). Therapeutic doses of albendazole, and ivermectin did not induce clinically important adverse reactions in sheep. One week later same animals were re-arranged again into two treatment groups each of eight sheep. Animals in the first group (C) were treated with Tetramisole 5% at dose rate 3mg/kg bwt and animals in the second group (D) were treated with Levamisole 2.5% at dose rate 7.5mg/kg bwt. Results indicated that the two anthelmintics (Tetramisole 5% and

Levamisole 2.5%) appeared equally ineffective as the first two drugs (Albendazole 2.5% and Ivermectin 0.8%). Likewise, there were no significant reductions in egg count in the four drugs used in the current study. These findings represent the first report in Sudan from the field of multiple anthelmintics resistance having developed in more than one drug after being administered to sheep. The study recommends further evaluation of the status of anthelmintic resistance in sheep using in vitro methods and molecular techniques.

المستخلص

عدة تقارير من انحاء متفرقة من السودان اشارت الي نقصان فعالية مضادات الديدان عند استخدامها في علاج الضان، تم استخدام اختبار الاختزال في عدد البيوض لقياس فعالية اربعة من مضادات الديدان شائعة الإستخدام وسط المرابين في الضان. فى الدراسة الحالية؛ تم استخدام عدد (16) من ذكور الضان المصابة طبيعياً بالديدان الاسطوانية لتقييم فعالية عقار البندازول 2.5 % المعد للتجريب و مقارنة النتائج مع عقار الايفرمكتين 0.8% المعد للتجريب. عينات من المستحضرات الدوائية (نفس التشغيلات) تم اختيارها عشوائياً واختبارها لضمان مطابقة المنتج النهائى للمواصفات قبل بداية التجربة. تم تقسيم الحيوانات الي مجموعتين بواقع ثمانية حيوانات لكلاً، المجموعة الاولى (أ) تم علاجها بعقار البندازول عن طريق الفم بجرعة واحدة مقدارها 5 مجم لكل كيلوجرام من من وزن الجسم. بينما تم علاج الحيوانات في المجموعة الثانية (ب) بعقار الايفرمكتين عن طريق الفم بجرعة واحدة مقدارها 0.2 مجم لكل كيلوجرام من وزن الجسم. تم تجميع عينات الروث في الفترات الزمنية التالية: الزمن صفر (قبل اعطاء الدواء) ثم في اليوم الثاني و الثالث و الرابع و السابع و العاشر و الرابع عشر و الحادي والعشرون (عقب العلاج). ايضا تم تجميع عينات الدم لاستقصاء اثر العلاج علي بعض مؤيضات الدم: البروتين الكلي، الزلال، انزيم الالنين امينو ترانسفيريز والاسبارتيت امينو ترانسفيريز، الكالسيوم، الفسفور و اليوريا. النتائج التي تم الحصول عليها اشارت الي انه لم يك هناك دليل لوجود فعالية للعلاج في المجموعتين (البندازول و الايفرمكتين). لم يك هناك اي اثر اكلينيكي علي مؤيضات الدم يشير الي اثار سامة للعقارين قيد الدراسة. بعد اسبوع من الدراسة الأولى تم إعادة توزيع وتقسيم الحيوانات لمجموعتين؛ ثمانية حيوانات لكل مجموعة، حيوانات المجموعة الأولى (ج) تم علاجها بعقار التتراميزول 5% عن طريق الفم بجرعة واحدة مقدارها 3 مجم لكل كيلوجرام من وزن الجسم، بينما تم علاج حيوانات بالمجموعة الثانية (د) بعقار الليفاميزول 2.5% عن طريق الفم بجرعة واحدة مقدارها 7.5 مجم لكل كيلو جرام من وزن الجسم. مره أخرى أوضحت النتائج عدم فعالية المستحضرين (التتراميزول 5% والليفاميزول 2.5%) لدرجة مقارنة لما حدث مع المستحضرين الآخرين (البندازول 2.5% والايفرمكتين 0.8%). لم يتم ملاحظة اي اختزال ذو دلالة معنوية في عدد البيوض عقب استخدام المستحضرات الاربعة. هذه النتائج تمثل أول

تقرير من الحقل بالسودان لمقاومة متعددة لمضادات الديدان لأكثر من مستحضر بعد ان تم تجريعها للضأن. توصي الدراسة بمزيد من التقصي عن حالة مقاومة الديدان للادوية باستخدام طرق مختبرية و طرق الاحياء الجزيئية.