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BIBLIOGRAFIA

Tema: IVERMECTIN Farmacocinetica

Fecha: 11/11/99

117:124059
Efficacy of ivermectin against infection of gastrointestinal nematodes in sheep.
Maru, A.; Srivastava, C. P.; Dubey, S. C. (Div. Anim. Health., CSWRI, Rajasthan 304 501, India). Indian J. Parasitol., 14(2), 241-2 (English) 1990. CODEN: IJPAES. ISSN: 0253-7168. DOCUMENT TYPE: Journal CA Section: 1 (Pharmacology)

118:139013
Ivermectin, an antiparasitic agent.
Campbell, William C. (Charles A. Dana Res. Inst., Drew Univ., Madison, NJ 07940, USA). Med. Res. Rev., 13(1), 61-79 (English) 1993. CODEN: MRREDD. ISSN: 0198-6325. DOCUMENT TYPE: Journal; General Review CA Section: 1 (Pharmacology)
A review with 57 refs.chem,fermn,mode of action , toxicol.,pharmacol.,antiparasitic activity ,etc. of ivermectin are discussed.

Vet Med Small Anim Clin 1981 Jun;76(6):877-9

The effectiveness of ivermectin for reducing bovine gastrointestinal helminthiasis.

Yazwinski TA, Greenway T, Williams M

Vet Rec 1980 Sep 6;107(10):226-7

Anthelmintic efficiency of ivermectin against naturally acquired bovine gastrointestinal nematodes.

Armour J, Bairden K, Preston JM

Ivermectin, one of the new avermectin group of anthelmintics, was more than 99 per cent effective in removing all stages of Ostertagia ostertagi including inhibited larvae, and adult Trichostrongylus axei when administered to cattle orally at 100 microgram/kg body-weight or subcutaneously at 100 and 200 microgram/kg body-weight. High efficacy (> 98.6 per cent) was also obtained against adults and inhibited larvae of Cooperia oncophora at 100 microgram/kg orally or 200 microgram/kg by subcutaneous injection. The latter treatment caused an 82.3 per cent reduction of adult Nematodirus helvetianus.

Title
Residual nematocidal effectiveness of ivermectin in cattle.
Author(s)
Yazwinski, T.A.
Featherston, H.
Johnson, Z.
Journal Info
American journal of veterinary research.
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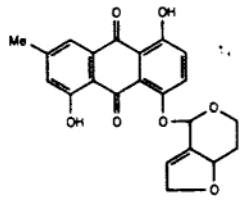
1416

reverse transcriptase. However, compds. belonging to the benzo= phenanthridine and protoberberine classes of alkaloids, certain flavanoids, the iridoid, fulvoplumierin, and the ansamycin antibiotic, daunomycin, exhibited similar potencies in both enzyme systems. In contrast, HIV-2 reverse transcriptase was obsd. to be four-fold more sensitive toward the inhibitory effects of the ipecac alkaloids, *O*-methylpsychotrine sulfate heptahydrate and psychotrine dihydrogen oxalate. Such differences in susceptibilities to inhibitors may indicate subtle dissimilarities in enzyme structure and function.

117: **124049b Lack of activity of amphotericin B in systemic murine fusarial infection.** Anaissie, Elias J.; Hachem, Ray; Legrand, Catherine; Legenne, Philippe; Nelson, Paul; Bodey, Gerald P. (M. D. Anderson Cancer Cent., Univ. Texas, Houston, TX USA). *J. Infect. Dis.* **1992,** 165(6), 1155–7 (Eng). Systemic fusarial infections are a significant cause of mortality in cancer patients. The antifungal activity of amphotericin B was studied in CF_1 mice with disseminated fusarial infections. Two pathogenic strains of *Fusarium solani* were used. I.p. administration of amphotericin B in daily doses of 0.5, 1, and 2 mg/kg for ≤10 days did not prolong the survival of treated animals. Clearance of *F. solani* from kidneys was similar in mice treated with 1 mg/kg/day and in untreated animals. The results agree with the known in vitro and in vivo resistance of *Fusarium* species to amphotericin B.

117: **124050v Antibacterial efficacy of a newly discovered antibiotic, MT81, in mice.** Chatterjee, T. K.; Chakravorty, A. (Dep. Pharm. Technol., Jadavpur Univ., Calcutta, 700 032 India). *Med. Sci. Res.* **1992,** 20(12), 459–60 (Eng). The ability of MT81 (I)



I

to protect mice infected with LDs of Gram-pos. bacteria is reported.

117: **124051w Study of suppressive effect of intravenous fluconazole on endogenous Candida endophthalmitis in rabbits.** Isobe, Yutaka; Hatano, Hiroshi (Sch. Med., Yokohama City Univ., Yokohama, Japan 236). *Jpn. J. Ophthalmol.* **1992,** 36(1), 23–7 (Eng). The effect of i.v. fluconazole on endogenous *Candida* endophthalmitis in rabbits were investigated. Preventive and therapeutic expts. were carried out. In the preventive series, rabbits were injected i.v. with 5 mg/kg of fluconazole at 30 min, 1 day and 2 days after i.v. inoculation with *C. albicans* spores. The control group received no medication. No treated rabbits developed ocular lesions and no *Candida* spores were isolated from the treated eyes. On the other hand, all control rabbits developed bilateral chorioretinitis and *C. albicans*, was isolated invariably from the control eyes. In the therapeutic series, i.v. fluconazole (5 mg/kg) was administered from 3 to 6 days after inoculation. All rabbits developed chorioretinitis and *Candida* spores were isolated from all eyes. Therefore, the results of this study prove that i.v. fluconazole is more effective in preventive use than in therapeutic use against endogenous *Candida* endophthalmitis in rabbits.

117: **124052x 3'-O-Benzyl-(E)-5-(2-bromovinyl)-2'-deoxyuridine is active as an anti-herpes agent in vivo but not in vitro.** De Clercq, E.; Walker, R. T.; Whale, R. F. (Rega Inst. Med. Res., Katholl. Univ. Leuven, B-3000 Louvain, Belg.). *Med. Chem. Res.* **1992,** 2(2), 111–18 (Eng). 3'-*O*-Benzyl-(*E*)-5-(2-bromovinyl)-2'-= deoxyuridine (3'-*O*-benzyl-BVDU) is a rare example of an antiviral agent, that, while inactive against herpes simplex virus type 1 (HSV-1) replication in murine or human cell cultures, proved almost as effective as its parent (BVDU), upon topical or oral administration, in suppressing HSV-1 infection in mice.

117: **124053y Influence of 12 antibiotics on antitumor immunity in BALB/c-mice.** Roszkowski, K.; Beuth, J.; Ko, H. L.; Roszkowski, W.; Jeljaszewicz, J.; Pulverer, G. (Inst. Lung Dis., Warsaw, Pol.). *Zentralbl. Bakteriol.* **1992,** 276(2), 280–7 (Eng). The effects of a 7-day chemotherapy with penicillin G, piperacillin, mezlocillin, cefalotin, cefamandole, cefotaxime, gentamicin, amikacin, streptomycin, rifampicin, doxycycline, and clindamycin on local tumor growth and metastatic lung colonization were studied in BALB/c mice bearing sarcoma L-1. The antibiotic doses were calcd. on a body wt. basis from doses recommended for human therapy. Except for mezlocillin, piperacillin, rifampicin, and doxycycline, the antibiotics did not influence the local tumor growth, lung colonization, and immune functions. Whereas mezlocillin exerted pos. (tumor suppressive) or neg. (tumor-promoting) effects depending on the chemotherapy schedule, tumor growth and spread were increased independently of the timing scheme after rifampicin or doxycyclin treatments. Since certain immune functions (delayed type hypersensitivity; proliferation of spleen lymphocytes) were suppressed after the administration of mezlocillin, rifampicin, and doxycycline, a correlation between antimicrobial chemotherapy and tumor progression may be possible.

117: **124054z Anthelmintic effect of an injectable formulation of praziquantel on cestodes in dogs and cats.** Fukase, Tohru; Suzuki, Makoto; Ogawa, Hitoshi; Chinone, Shiro; Akihama, Sumiyuki (Fac. Pharm., Meiji Coll. Pharm., Nozawa, Japan 154). *Nippon Juishikai Zasshi* **1992,** 45(6), 408–13 (Japan). An injectable formulation of praziquantel (Droncit injectable, Bayer Japan Ltd., Tokyo, Japan) was evaluated for the anthelmintic effect on cestodes in dogs and cats. Twelve cats inoculated orally with 3 plerocercoids of *Spirometra erinacei* were divided into 4 group of 3 animals each consisting of one nontreated control and 3 medicated groups. The medicated groups were injected s.c. and i.m. with the injectable formulation. One medicated group was administered orally with a tablet of praziquantel (Droncit tablet, Bayer Japan Ltd., Tokyo, Japan). The dosage level was 30 mg active ingredient per kg body wt. which was detd. 20 days after infection. The anthelmintic was completely effective against *S. erinacei* in all medicated cats and there was no difference in the efficacy among the administrating methods. In subsequently executed clin. trials, s.c. and i.m. injections of the injectable formulation completely eliminated cestodes from all treated animals: 36 dogs and 27 cats naturally infected with *Dipylidium caninum*, 2 dogs with *Taneia* sp. and 1 cat with *T. taeniaeformis* in a dose of 0.1 mL product (=5.68 mg active ingredient) per kg body wt. and 12 dogs and 22 cats with *S. erinacei* in a dose of 0.6 mL (=34.08 mg)/kg. These results confirm that s.c. and i.m. injections of praziquantel resulted in the same complete efficacy as that by oral administration against cestodes in dogs and cats.

117: **124055a In vivo and in vitro effects of methacrylanilides and acetylcarboxanilide on akaline phosphatase activity of Echinococcus multilocularis metacestodes.** Audin, P.; Sarciron, M. E.; Paris, J.; Petavy, A. F. (Groupe Rech. Antiparasit., Fac. Pharm., 69373 Lyon, Fr.). *Eur. J. Med. Chem.* **1992,** 27(3), 285–9 (Eng). In search for effective chemotherapy of alveolar hydratid disease key enzymes of *Echinococcus multilocularis* metacestodes were investigated. Isatin (2,3-indolinedione) is well known as an inhibitor of alk. phosphatase activity, and has been previously investigated. Acetylcarboxanilide, an 'open drug' of isatin, and 2 methacrylanilides were evaluated for their ability to inhibit alk. phosphatase activity of *Echinococcus multilocularis* metacestodes in vivo. These 'open drugs' are more efficient than isatin, and *p*-chloromethacrylanilide exhibits a strong selectivity for the parasite enzyme and is also effective in vitro. The results obtained with *p*-chloromethacrylanilide are promising.

117: **124056b Tetracyclines (TETs) inhibit the synthesis and/or activity of cartilage proteinases in vivo and in vitro.** Arsenis, Charalampos; Moak, Susan A.; Greenwald, Robert A. (Ciba-Geigy Res. Dep., Summit, NJ USA). *Matrix Metalloproteinases Inhib., Proc. Matrix Metalloproteinase Conf.* 1989 (Pub. **1992**), 314 (Eng). Edited by Birkedal-Hansen, Henning. Fischer: Stuttgart, Germany. Tetracyclines are effective inhibitors of connective tissue degrading matrix metalloproteinases. Their antibiotic usefulness in connective tissue diseases is due to this phenomena.

117: **124057c Effect of thiabendazole and mebendazole on certain biochemical parameters of Nippostrongylus brasiliensis infected albino rats.** Misra, Anuradha; Srivastava, Arvind K. (Div. Parasitol. Biochem., Cent. Drug Res. Inst., Lucknow, 226001 India). *Indian J. Parasitol.* **1990,** 14(2), 125–7 (Eng). Levels of blood glucose, serum lactic acid, and activities of acid phosphatase, alk. phosphatase, glutamic oxaloacetic transaminase and glutamic pyruvic transaminase in *N. brasiliensis* infected albino rats before and after treatment with thiabendazole (TBZ) and mebendazole (MBZ) were measured. Treatment with TBZ gave interesting results where blood glucose and serum lactic acid levels rose with assocd. increase in the activities of acid phosphatase, glutamic oxaloacetic and glutamic pyruvic transaminases. No such changes were obsd. after treatment with MBZ. Alk. phosphatase activity, however, was depressed in both the cases. It, therefore, appears that TBZ causes stress on the liver which apparently increases its glycogenolysis and mobilization of acid phosphatase and transaminases, resp.

117: **124058d Comparative efficacy of anthelmintics against moneiziasis in sheep.** Gill, J. S.; Bali, H. S.; Miglani, A. (Coll. Vet. Sci., Punjab Agric. Univ., Ludhiana, 141 004 India). *Indian J. Parasitol.* **1990,** 14(2), 137–9 (Eng). A comparative efficacy of albendazole, mebendazole, nidosamide, and fenbendazole against *Moneizia* infection was evaluated in sheep.

117: **124059e Efficacy of ivermectin against infection of gas= trointestinal nematodes in sheep.** Maru, A.; Srivastava, C. P.; Dubey, S. C. (Div. Anim. Health., CSWRI, Rajasthan, 304 501 India). *Indian J. Parasitol.* **1990,** 14(2), 241–2 (Eng). This study confirmed the efficacy of ivermectin at the recommended dose rate. It was found to be 100% effective against natural nematode infection in sheep. Ivermectin can be used in sheep flocks because of its ease in administration and efficacy against common sheep nematodes.

117: **124060y Poly(hydroxy)carboxylates as selective inhibitors of cytomegalovirus and herpes simplex virus replication.** Neyts, J.; Snoeck, R.; Wutzler, P.; Cushman, M.; Kloecking, R.; Helbig, B.; Wang, P.; De Clercq, E. (Rega Inst. Med. Res., Kathol. Univ. Leuven, B-3000 Louvain, Belg.). *Antiviral Chem. Chemother.* **1992,** 3(4), 215–22 (Eng). Polyhydroxycarboxylates (MW 3800–14000) derived from phenolic (PDP) compds. were found to be selective inhibitors of human cytomegalovirus (CMV), herpes simplex virus type 1 (HSV-1), type 2 (HSV-2), thymidine kinase-deficient (TK⁻) HSV-1 and vaccinia virus replication at concns. that are not toxic to the host cells. The PDP compds. were not inhibitory to parainfluenza virus, reovirus, Sindbis virus, or Semliki forest virus. The polycarboxylate aurintricarboxylic acid (ATA) (MW 1149–3336) also proved inhibitory to CMV and HSV replication. The anti-CMV and anti-HSV activities of the ATA polymers increased with increasing mol. wt. The mechanism of anti-CMV activity of both the PDP and ATA series of compds. can be attributed to the inhibition of virion attachment to the cells, probably due to an interaction of these polyanionic compds. with the pos. charged domains of the viral envelope glycoproteins.

121: 271377t **Scar formation in the vestibular sensory epithelium after aminoglycoside toxicity.** Meiteles, Lawrence Z.; Raphael, Yehoash (Medical Center, University of Michigan, Ann Arbor, MI 48109-0506 USA). *Hear. Res.* **1994**, 79(1-2), 26-38 (Eng). Hair cell degeneration and the repair process due to differing types of trauma have been studied extensively in the organ of Corti. It has been detd. that, during scar formation, after differing types of trauma to the auditory sensory system, the reticular lamina is maintained with adherens junctions and tight junctions. We investigated the repair process within the vestibular epithelium. Hair cell degeneration was induced by the unilateral application of streptomycin to the inner ears of guinea pigs. Whole mount prepns. of all five vestibular organs were processed and examd. by fluorescence, light and electron microscopy. Scar formation was seen as early as 4 days post-treatment with streptomycin and was noted to coincide with hair cell degeneration. Neighboring supporting cells swelled and filled the space beneath the degenerating hair cell. Between three and five supporting cells participate in the reparative process. The distribution of cytokeratin is also altered during scar formation. The area once occupied by the hair cell becomes filled with cytokeratin-rich processes of supporting cells. It appears that differing nos. of supporting cells are involved in the reparative process within the vestibular sensory epithelium as compared to the auditory system. The reticular lamina remains intact at all times. This may possibly prevent mixing of fluids between different compartments in the inner ear and dysfunction of the vestibular sensory organs.

121: 271378u **liver reactions from trimethoprim.** Lindgren, A.; Olsson, R. (Department of Medicine, Sahlgrenska University Hospital, Goeteborg, Swed.). *J. Intern. Med.* **1994**, 236(3), 281-4 (Eng). The objective of the study is to det. whether there are adverse liver reactions to trimethoprim and, if found, to describe the biochem. pattern of these reactions. The authors surveyed all liver reactions from trimethoprim reported to SADRAC (Swedish Adverse Drug Reactions Advisory Committee) from 1980 to 1989. During 1980-1989, 21 suspected liver reactions from trimethoprim were reported. A causal relation was considered probable in 10 of these reports, which gives an incidence of 1/1360000 DDD. The distribution of reaction types for trimethoprim was virtually identical to that found in corresponding adverse reports for trimethoprim-sulfonamides, whereas the sulfonamides as single drugs displayed a significantly higher proportion of more severe hepatocellular reactions.

121: 271379v **Ultrastructural localization of calcium in neuromuscular junctions of smooth and skeletal muscles after aminoglycoside antibiotics treatment.** Nouhnejad, P.; Dehpour, A.R.; Samadian, T.; Amini, Sh. (Pharmaceutical Research Center, Darou Pakhsh Co., Iran). *Histol. Histopathol.* **1994**, 9(3), 555-61 (Eng). Aminoglycoside antibiotics are all capable of producing clin. significant neuromuscular paralysis. Since part of the mechanism of action of these antibiotics at the neuromuscular junction is a calcium-dependent inhibition of acetylcholine release, this expt. was carried out in vitro on both somatic (isolated rat phrenic-nerve hemidiaphragm) and autonomic neuro-effector transmission (guinea-pig ileum) using gentamicin and amikacin, to det. the calcium contents at this level. Electron microscopic observations on gentamicin- and or amikacin-treated materials, using the potassium pyroantimonate method, suggest a redn. of internal calcium in nerve terminals of both prepns.

121: 271380p **Clinical and laboratory studies of the photosensitizing potential of norfloxacin, a 4-quinolone broad-spectrum antibiotic.** Ferguson, J.; Johnson, B.E. (Department of Dermatology, University of Dundee, Dundee, UK DD1 9SY). *Br. J. Dermatol.* 1993, 128(3), 285-95 (Eng). Cutaneous photosensitivity reactions are a consistent although uncommon feature of the fluoroquinolone group of antibiotics, which are related to nalidixic acid. Objective lab. and clin. data are now routinely required by regulatory bodies for new drugs suspected of being photosensitizers, but no clear recommendations exist. A series of in vitro tests ranging in complexity revealed a UVA-dependent phototoxic potential for the fluoroquinolone norfloxacin similar to that for ciprofloxacin, and less than that of nalidixic acid. Controlled monochromator phototesting, designed to reveal the clin. characteristics, wavelength dependence and severity of cutaneous reactions in normal subjects showed both norfloxacin and ciprofloxacin to have a weak phototoxic potential which clears within 4 wk of stopping the drug. UVA wavelengths (335±30 nm; 365±30 nm) appear most responsible for producing an asymptomatic erythema which is maximal at 24 h. The clin. study differs from those used previously in being blind, contg. pos. and neg. controls, and phototesting after cessation of drug intake. The methodol. has the anticipated limitation of failing to detect idiosyncratic photosensitivity responses.

121: 271381q **Closantel: myoneural activity and mechanism of fasciolicidal activity.** Elmallah, Ahmed I.; Abdel-Aziz, Mostafa; Elsawy, Abdel-Salam F.; Elashmawy, Ibrahim M. (Faculty of Pharmacy, University of Alexandria, Alexandria, Egypt). *Alexandria J. Pharm. Sci.* **1994**, 8(2), 89-93 (Eng). Closantel, a recently introduced fasciolicidal drug, was tested on a no. of skeletal muscle prepns. in a trial to explore its effect on the neuromuscular transmission and to explain the mechanism of its fasciolicidal activity. On the chick biventer cervicis muscle, closantel induced irreversible neuromuscular blockade accompanied by slowly developing contracture. Closantel, however, slightly reduced carbachol-induced contracture. On the rat hemi-diaphragm, closantel potentiated the elec. evoked muscle twitches followed by irreversible neuromuscular blockade. Neither neostigmine nor calcium chloride could reverse the established neuromuscular blockade. Closantel induced significant contracture of the diaphragm muscle which was not affected by pretreatment with dantrolene, TMB-8, diltiazem or tubocurarine. On the frog rectus abdominis muscle, closantel induced a well defined contracture which was not affected by tubocurarine. At the same time, closantel failed to affect ACh-induced contracture of the muscle. Closantel also caused initial stimulation of the motility of Fasciola gigantica worms manifested as increase in the tone and frequency of contraction. This was followed by irreversible spastic paralysis. The drug also significantly inhibited the activity of total cholinesterase enzyme obtained from Fasciola gigantica homogenates. It was concluded that closantel possesses a pronounced non-specific neuromuscular blocking activity, which might be related to its reported capacity to uncouple mitochondrial oxidative phosphorylation.

121: 271382r **Reduction in replication of the human immunodeficiency virus type 1 in human T cell lines by polymerase III-driven transcription of chimeric tRNA-antisense RNA genes.** Junker, Uwe; Rittner, Karola; Homann, Matthias; Bevec, Dorian; Bohnlein, Ernst; Sczakiel, Georg (Wien, Austria). *Antisense Res. Dev.* **1994**, 4(3), 165-72 (Eng). Inhibition of human immunodeficiency virus type 1 (HIV-1) replication was demonstrated by using tat- and rev-directed antisense oligoribonucleotides 68 and 69 nucleotides in length. In this study, human T-lymphoid cells were transduced with a murine amphotropic retroviral vector contg. a polymerase III-driven chimeric gene consisting of the human $tRNA_i^{met}$ sequence and the short tat- and rev-directed antisense sequences that had been shown before to inhibit HIV-1 replication. Pools of transduced, G418-resistant human T-lymphoid Jurkat or CEM cells showed reduced replication of HIV-1 in the presence of antisense-contg. chimeric transcripts, but not with sense sequence-contg. transcripts. These results demonstrate that short inhibitory antisense RNA transcripts can be stably expressed endogenously using polymerase III promoters, which can reduce replication of HIV-1. The approach described in this work combines the advantages of short and, usually, synthetic oligonucleotides with the stable intracellular expression of inhibitory genes for HIV-1 in target cells. Considering the small size of the described chimeric polymerase III genes, it appears feasible to combine multiple antiviral genes with the currently available retroviral vectors as gene delivery systems.

121: 271383s **Effects of a traditional Chinese herbal medicine, Kanzo-bushi-to, on the resistance of thermally injured mice infected with herpes simplex virus type 1.** Matsuo, Ryuichi; Ball, Michael A.; Kobayashi, Makiko; Herndon, David N.; Pollard, Richard B.; Suzuki, Fujio (Dep. Internal Med., Univ. Texas Med. Branch, Galveston, TX 77555-0882 USA). *Int. J. Immunopharmacol.* **1994**, 16(10), 855-63 (Eng). The protective effect of Kanzo-bushi-to (TJS-038) was investigated on the opportunistic infection of herpes simplex virus type 1 (HSV) in thermally injured mice (TI-Mice). The authors have previously reported that TI-Mice were approx. 100 times more susceptible to HSV infection than normal mice (N-Mice) and that $CD8^+$ suppressor T (ST)-cells induced by burn injury were involved in causing this increased susceptibility of TI-Mice. Increased susceptibility of TI-Mice to the infection was reversed to the levels obsd. in N-Mice when TI-Mice were treated i.p. with TJS-038 at a dose of 5 mg/kg 1 and 4 days after thermal injury. The activity of ST-cells was greatly decreased in TI-Mice treated with TJS-038. The generation of Vicia villosa lectin-adherent $CD4^+$ $CD28^+$ TCR-α/β^+ contrasuppressor T (Contra-ST)-cells assocd. with the appearance of ST-cells was expanded and occurred earlier in spleens of TJS-038-treated TI-Mice as compared with that of untreated TI-Mice. The improved resistance of TJS-038-treated TI-Mice to the infection was transferred to untreated TI-Mice by adoptive transfer of Contra-ST-cells prepd. from TJS-038-treated TI-Mice. These results suggest that TJS-038 may restore the resistance of TI-Mice to the HSV infection through the expanded generation of Contra-ST-cells.

121: 271384t **Synthesis and anti-HIV activity of poly(cysteic acid).** Oh, Young-im; Cushman, Mark (Dep. Med. Chem. Pharmacognosy, Purdue Univ., West Lafayette, IN 47907 USA). *Bioorg. Med. Chem. Lett.* **1994**, 4(18), 2245-8 (Eng). Poly(cysteic acid) was synthesized and found to inhibit the cytopathic effect of HIV-1 in CEM cell cultures at concns. that were not cytotoxic to uninfected CEM cells.

121: 271385u **Residual nematocidal effectiveness of ivermectin in cattle.** Yazwinski, T. A.; Featherston, H.; Tucker, C.; Johnson, Z. (Department of Animal Sciences, University of Arkansas, Fayetteville, AR 72701 USA). *Am. J. Vet. Res.* **1994**, 55(10), 1416-20 (Eng). We assessed the duration of ivermectin persistence by measuring posttreatment nematocidal effectiveness; topical and injectable formulations of ivermectin were evaluated. Thirty-five nematode-free calves were randomly allocated to 1 of 5 treatment groups (7 calves/group). The treatment (Trt) group designations were: Trt 1, nonmedicated; Trt 2, injectable ivermectin administered at the rate of 0.2 mg/kg of body wt. on day 0; Trt 3, injectable ivermectin administered at the aforementioned rate, but on day 7; Trt 4, topically administered ivermectin at the rate of 0.5 mg/kg on day 0; and Trt 5, topically administered ivermectin at the aforementioned rate, but on day 7. All calves were subsequently given infective larvae of Haemonchus, Cooperia, Trichostrongylus, and Oesophagostomum spp on day 21. One week later, each calf was addnl. administered infective larvae of Dictyocaulus and Ostertagia spp. Trial calves were euthanatized on trial days 49 to 52 for nematode quantitation. On the basis of geometric mean comparisons, total nematode burdens were reduced from control group counts by 98.9 and 86.3% for calves treated on days 7 and 0 with injectable formulations, resp., and 97.2 and 64.7% for calves treated on days 7 and 0 with pour-on formulations, resp. Trichostrongylus colubriformis infections were most refractory to the persistent activity of ivermectin, with H.

Vet Res 1993;24(5):417-21

Ivermectin in goat plasma and milk after subcutaneous injection.

Alvinerie M, Sutra JF, Galtier P

Station de pharmacologie-toxicologie, Toulouse, France.

The pharmacokinetics and mammary excretion of ivermectin were determined in goats following a single sc administration (0.2
mg/kg). Kinetic analysis of plasma and milk levels was performed using a 1-compartment model. The maximum plasma
concentration of 6.12 ng/ml occurred at 2.85 d; the half-life of 4.03 d was similar to the value in sheep (3.68 d). Ivermectin was
detected in the milk at the first sampling time and thereafter for at least 25 d. Comparison of the milk and plasma data shows the
parallel disposition of the drug in milk and plasma with a milk-plasma concentration ratio of 1.08 +/- 0.23. In conclusion, the
persistence of the drug in plasma is reflected in the duration of the presence of ivermectin in milk.

J Pharm Sci 1985 Oct;74(10):1105-7

Pharmacokinetics of ivermectin administered intravenously to cattle.

Wilkinson PK, Pope DG, Baylis FP

Ivermectin, a macrocyclic lactone disaccharide antiparasitic agent, was administered intravenously to six young calves (one bull,
five steers) as a bolus dose of 200 micrograms/kg. The disposition kinetics of ivermectin in cattle can be described by a
three-compartment open model with elimination from the central compartment. Compartmental analysis yielded mean parameters
as follows: terminal elimination rate constant (beta) = 0.258 d-1, biological half-life (t 1/2 beta) = 2.7 d; apparent volume of
distribution of the central compartment (Vd1) = 0.45 L/kg; apparent volume of distribution at steady state (Vdss) = 2.4 L/kg. The
area under the plasma concentration-time curve (AUC) was 254 ng X d/mL. Noncompartmental parameters, obtained by utilizing
statistical moment theory, mean residence time (MRT), clearance (CL), and Vdss were calculated to be 2.8 d, 0.79 L/kg X d, and
2.2 L/kg, respectively.

Vet Parasitol 1999 Oct 1;86(3):203-15

Ivermectin disposition kinetics after subcutaneous and intramuscular administration of an oil-based formulation to cattle.

Lifschitz A, Virkel G, Pis A, Imperiale F, Sanchez S, Alvarez L, Kujanek R, Lanusse C

Departamento de Fisiopatologia, Facultad de Ciencias Veterinarias, Universidad Nacional del Centro, Campus Universitario,
Tandil, Argentina.

Slight differences in formulation may change the plasma kinetics and ecto-endoparasiticide activity of endectocide compounds.
This work reports on the disposition kinetics and plasma availability of ivermectin (IVM) after subcutaneous (SC) and
intramuscular (IM) administration as an oil-based formulation to cattle. Parasite-free Aberdeen Angus calves (n = 24; 240-280 kg)
were divided into three groups (n = 8) and treated (200 microg/kg) with either an IVM oil-based pharmaceutical preparation
(IVM-TEST formulation) (Bayer Argentina S.A.) given by subcutaneous (Group A) and intramuscular (Group B) injections or the
IVM-CONTROL (non-aqueous formulation) (Ivomec, MSD Agvet) subcutaneously administered (Group C). Blood samples were
taken over 35 days post-treatment and the recovered plasma was extracted and analyzed by HPLC using fluorescence detection.
IVM was detected in plasma between 12 h and 35 days post-administration of IVM-TEST (SC and IM injections) and
IVM-CONTROL formulations. Prolonged IVM absorption half-life ($p < 0.05$) and delayed peak plasma concentration ($p < 0.001$)
were obtained following the SC administration of the IVM-TEST compared to the IVM-CONTROL formulation. No differences
in total plasma availability were observed among treatments. However, the plasma residence time and elimination half-life of IVM
were significantly longer after injection of the IVM-TEST formulation. IVM plasma concentrations were above 0.5 ng/ml for 20.6
(CONTROL) and 27.5 days (IVM-TEST SC), respectively ($p < 0.05$). The modified kinetic behaviour of IVM obtained after the
administration of the novel oil-based formulation examined in this trial, compared to the standard preparation, may positively impact
on its strategic use in cattle.

Publication Types:

Clinical trial
Randomized controlled trial

J Vet Pharmacol Ther 1985 Mar;8(1):88-94

Pharmacokinetics of ivermectin in sheep following intravenous, intra-abomasal or intraruminal administration.

Prichard RK, Steel JW, Lacey E, Hennessy DR

The pharmacokinetics of ivermectin in plasma following intravenous, intra-abomasal, and intraruminal administration to sheep was
determined. When given intravenously, ivermectin was very slowly eliminated with a terminal half-life of 178 h and a volume of
distribution at steady state of 5.3 l/kg indicating sequestration in a temporary depot. Intra-abomasal administration resulted in rapid
absorption, a peak plasma concentration of 60.6 ng/ml at 4.4 h, and 100% bioavailability. However, intraruminal administration
produced a much lower peak concentration (17.6 ng/ml at 23.5 h) and bioavailability (25.1%). A subsequent in vitro study
indicated that ivermectin may be rapidly metabolized in the rumen.

Vet Med Small Anim Clin 1981 Jun;76(6):877-9

The effectiveness of ivermectin for reducing bovine gastrointestinal helminthiasis.

Yazwinski TA, Greenway T, Williams M

Vet Rec 1980 Sep 6;107(10):226-7

Anthelmintic efficiency of ivermectin against naturally acquired bovine gastrointestinal nematodes.

Armour J, Bairden K, Preston JM

Ivermectin, one of the new avermectin group of anthelmintics, was more than 99 per cent effective in removing all stages of Ostertagia ostertagi including inhibited larvae, and adult Trichostrongylus axei when administered to cattle orally at 100 microgram/kg body-weight or subcutaneously at 100 and 200 microgram/kg body-weight. High efficacy (> 98.6 per cent) was also obtained against adults and inhibited larvae of Cooperia oncophora at 100 microgram/kg orally or 200 microgram/kg by subcutaneous injection. The latter treatment caused an 82.3 per cent reduction of adult Nematodirus helvetianus.

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Normal phase liquid chromatographic determination of nanogram quantities of ivermectin in cattle blood or plasma.

Schnitzerling HJ, Nolan J

A method has been developed for determining ivermectin in 5 mL samples of cattle blood by a 2-step process: cleanup solvent extraction followed by direct injection onto a normal phase liquid chromatography (LC) system with UV detection. Recovery was 77-80% +/- 5.5% standard deviation. Endogenous interference that may be present caused the lower limit of detection to be set at 4-5 ng/mL. The method was used to show that in blood the distribution of ivermectin favors plasma in a fixed proportion over cellular material, and further to provide a time-course profile of ivermectin in the whole blood of injected cattle. In whole blood, ivermectin concentration peaked between 3 and 5 days and dissipated slowly with a half-life of 3 days.

J Vet Pharmacol Ther 1999 Feb;22(1):27-34

Bioequivalence of ivermectin formulations in pigs and cattle.

Lifschitz A, Pis A, Alvarez L, Virkel G, Sanchez S, Sallovitz J, Kujanek R, Lanusse C

Departamento de Fisiopatologia, Facultad de Ciencias Veterinarias, Universidad Nacional del Centro, Tandil, Argentina.

The vehicle in which endectocide compounds are formulated plays a relevant role in their absorption kinetics and resultant systemic availability. The pharmaceutical bioequivalence and comparative plasma disposition kinetics of ivermectin (IVM), following the subcutaneous administration of two injectable formulations to pigs and cattle were investigated using parallel experimental designs. Sixteen parasite-free male Duroc Jersey-Yorkshire crossbred pigs (90-110 kg) (Expt 1) and 16 parasite-free male Holstein calves (100-120 kg) (Expt 2) were divided into two groups and treated subcutaneously at either 300 (pigs) or 200 (calves) microg/kg with two different propylene glycol/glycerol formal (60: 40) based IVM formulations; in both experiments pigs or calves in Group A received the test (IVM-TEST) formulation and those in Group B were treated with the reference formulation (IVM-CONTROL). Heparinized blood samples were taken from 0 h up to either 20 (pigs) or 30 (calves) days post-treatment and plasma was extracted, derivatized and analysed by high performance liquid chromatography (HPLC) using fluorescence detection. Early detection of IVM (12 h) with a peak plasma concentration (C(max)) between 33 and 39 ng/mL was observed in pigs. The drug was detected in plasma up to 20 days post-administration of either formulation,

resulting in elimination half-lives between 3.47 and 3.80 days. There were no differences between the IVM-TEST and
IVM-CONTROL formulations in the kinetic parameters (except t(max)) obtained in pigs. IVM was detected in plasma
between 12 h and 30 days post-administration of both formulations under investigation in cattle. The plasma disposition kinetics
of IVM in calves was similar following treatment with both formulations. C(max) values (between 40.5 and 46.4 ng/mL) were
achieved at 2 days post-administration of both formulations. None of the estimated kinetic parameters were statistically
different between drug formulations. The injectable IVM formulations investigated were bioequivalent after their subcutaneous
administration to both pigs and calves at recommended dose rates.

Vet Parasitol 1997 Sep;72(1):3-8

Comparative pharmacokinetics of doramectin and ivermectin in cattle.

Toutain PL, Upson DW, Terhune TN, McKenzie ME

Ecole Nationale Veterinaire de Toulouse, Unite associee INRA de Physiopathologie et Toxicologie Experimentales, Toulouse,
France.

Plasma pharmacokinetics were compared for 40 cattle dosed by subcutaneous injection with doramectin or ivermectin (200
micrograms kg-1), commercial formulations of doramectin or ivermectin, 20 cattle per product). Doramectin exhibited a similar
peak plasma concentration to ivermectin (about 32 ng ml-1), but the time to Cmax was longer for doramectin (5.3 +/- 0.35
days) than for ivermectin (4.0 +/- 0.28 days). The area under the curve from time 0 to infinity post-injection was significantly
higher ($p < 0.001$) for doramectin (511 +/- 16 ng day ml-1) than for ivermectin (361 +/- 17 ng day ml-1). This was explained
by a lower clearance, a lower volume of distribution and, probably, a higher bioavailability of doramectin over ivermectin. It is
concluded that the pharmacokinetic differences between doramectin and ivermectin may explain the longer duration of preventive efficacy of doramectin.

J Vet Pharmacol Ther 1997 Apr;20(2):91-9

Comparative plasma disposition kinetics of ivermectin, moxidectin and
doramectin in cattle.

Lanusse C, Lifschitz A, Virkel G, Alvarez L, Sanchez S, Sutra JF, Galtier P, Alvinerie M

Departamento de Fisiopatologia, Facultad de Ciencias Veterinarias, Universidad Nacional del Centro, Tandil, Argentina.

The persistence of the broad-spectrum antiparasitic activity of endectocide compounds relies on their disposition kinetics and
pattern of plasma/tissues exchange in the host. This study evaluates the comparative plasma disposition

kinetics of ivermectin
(IVM), moxidectin (MXD) and doramectin (DRM) in cattle treated with commercially available injectable formulations. Twelve
(12) parasite-free male Hereford calves (180-210 kg) grazing on pasture were allocated into three groups of four animals each.
Animals in each group received either IVM (Ivomec 1%, MSD AGVET, Rahway, NJ, USA), MXD (Cydectin 1%. American
Cyanamid, Wayne, NJ, USA) or DRM (Dectomax 1%, Pfizer Inc., New York, NY, USA) by subcutaneous injection at a
dose of 200 micrograms/kg. Jugular blood samples were collected from 1 h up to 80 days post-treatment, and plasma
extracted, derivatized and analysed by high performance liquid chromatography (HPLC) using fluorescence detection. The
parent molecules were detected in plasma between 1 h and either 70 (DRM) or 80 (IVM and MXD) days post-treatment. The
absorption of MXD from the site of injection was significantly faster (absorption half-life (t1/2ab) = 1.32 h) than those of IVM
(t1/2ab = 39.2 h) and DRM (t1/2ab = 56.4 h). MXD peak plasma concentration (Cmax) was reached significantly earlier
(8.00 h) compared to those of IVM and DRM (4-6 days post-treatment). There were no differences on Cmax values: the area
under the concentration-time curve (AUC) was higher for IVM (459 ng.d/mL) and DRM (627 ng.d/mL) compared to that of
MXD (217 ng.d/mL). The mean plasma residence time was longer for MXD (14.6 d) compared to IVM (7.35 d) and DRM
(9.09 d). Unidentified metabolites were detected in plasma: they accounted for 5.75% (DRM), 8.50% (IVM) and 13.8%
(MXD) of the total amount of their respective parent drugs recovered in plasma. The comparative plasma disposition kinetics
of IVM, MXD and DRM in cattle, characterized over 80 days post-treatment under standardized experimental conditions, is reported for the first time.

J Vet Pharmacol Ther 1995 Aug;18(4):290-8

Pharmacokinetics and bioequivalence of parenterally administered
doramectin in cattle.

Nowakowski MA, Lynch MJ, Smith DG, Logan NB, Mouzin DE, Lukaszewicz J, Ryan NI, Hunter RP, Jones RM

Pfizer Inc. Central Research Division, Groton, Connecticut 06340, USA.

Plasma concentrations of doramectin in 40 cattle dosed by subcutaneous (sc) or intramuscular (i.m.) injection (200
micrograms/kg) were compared to assess the bioequivalence of the two routes of administration. Peak concentration (Cmax),
and areas under the concentration curve (AUC0-infinity) were determined from plasma concentrations. Animals treated by the
sc route showed a mean AUC0-infinity of 457 +/- 66 ng.day/mL (+/- SD) and a mean Cmax of 27.8 +/- 7.9 ng/mL. Results
from the i.m. treatment group showed a mean AUC0-infinity of 475 +/- 82 ng.day/mL and a mean Cmax of 33.1 +/- 9.0

ng/mL. Absorption constants (ka) determined by modelling were 0.542 +/- 0.336 day-1 after sc administration and 0.710 +/-
0.357 day-1 after i.m. administration. The 90% confidence limits on the difference between mean AUC0-infinity values for the
sc and i.m. groups fell within 20% of the mean value for the subcutaneous group. Cmax was somewhat greater for the i.m.
route. The 90% confidence limits on the difference in mean In(Tmax +1) also fell within 20% of the mean sc value. Based on
this analysis, bioequivalence of the sc and i.m. formulation has been established.

Vet Parasitol 1999 Oct 1;86(3):203-15

Ivermectin disposition kinetics after subcutaneous and intramuscular administration of an oil-based formulation to cattle.

Lifschitz A, Virkel G, Pis A, Imperiale F, Sanchez S, Alvarez L, Kujanek R, Lanusse C

Departamento de Fisiopatologia, Facultad de Ciencias Veterinarias, Universidad Nacional del Centro, Campus Universitario,
Tandil, Argentina.

Slight differences in formulation may change the plasma kinetics and ecto-endoparasiticide activity of endectocide compounds.
This work reports on the disposition kinetics and plasma availability of ivermectin (IVM) after subcutaneous (SC) and
intramuscular (IM) administration as an oil-based formulation to cattle. Parasite-free Aberdeen Angus calves (n = 24; 240-280 kg)
were divided into three groups (n = 8) and treated (200 microg/kg) with either an IVM oil-based pharmaceutical preparation
(IVM-TEST formulation) (Bayer Argentina S.A.) given by subcutaneous (Group A) and intramuscular (Group B) injections or the
IVM-CONTROL (non-aqueous formulation) (Ivomec, MSD Agvet) subcutaneously administered (Group C). Blood samples were
taken over 35 days post-treatment and the recovered plasma was extracted and analyzed by HPLC using fluorescence detection.
IVM was detected in plasma between 12 h and 35 days post-administration of IVM-TEST (SC and IM injections) and
IVM-CONTROL formulations. Prolonged IVM absorption half-life ($p < 0.05$) and delayed peak plasma concentration ($p < 0.001$)
were obtained following the SC administration of the IVM-TEST compared to the IVM-CONTROL formulation. No differences
in total plasma availability were observed among treatments. However, the plasma residence time and elimination half-life of IVM
were significantly longer after injection of the IVM-TEST formulation. IVM plasma concentrations were above 0.5 ng/ml for 20.6
(CONTROL) and 27.5 days (IVM-TEST SC), respectively ($p < 0.05$). The modified kinetic behaviour of IVM obtained after the
administration of the novel oil-based formulation examined in this trial, compared to the standard preparation, may positively impact
on its strategic use in cattle.

Publication Types:

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Randomized controlled trial

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Ivermectin in goat plasma and milk after subcutaneous injection.

Alvinerie M, Sutra JF, Galtier P

Station de pharmacologie-toxicologie, Toulouse, France.

The pharmacokinetics and mammary excretion of ivermectin were determined in goats following a single sc administration (0.2
mg/kg). Kinetic analysis of plasma and milk levels was performed using a 1-compartment model. The maximum plasma
concentration of 6.12 ng/ml occurred at 2.85 d; the half-life of 4.03 d was similar to the value in sheep (3.68 d). Ivermectin was
detected in the milk at the first sampling time and thereafter for at least 25 d. Comparison of the milk and plasma data shows the
parallel disposition of the drug in milk and plasma with a milk-plasma concentration ratio of 1.08 +/- 0.23. In conclusion, the
persistence of the drug in plasma is reflected in the duration of the presence of ivermectin in milk.

J Pharm Sci 1985 Oct;74(10):1105-7

Pharmacokinetics of ivermectin administered intravenously to cattle.

Wilkinson PK, Pope DG, Baylis FP

Ivermectin, a macrocyclic lactone disaccharide antiparasitic agent, was administered intravenously to six young calves (one bull,
five steers) as a bolus dose of 200 micrograms/kg. The disposition kinetics of ivermectin in cattle can be described by a
three-compartment open model with elimination from the central compartment. Compartmental analysis yielded mean parameters
as follows: terminal elimination rate constant (beta) = 0.258 d-1, biological half-life (t 1/2 beta) = 2.7 d; apparent volume of
distribution of the central compartment (Vd1) = 0.45 L/kg; apparent volume of distribution at steady state (Vdss) = 2.4 L/kg. The
area under the plasma concentration-time curve (AUC) was 254 ng X d/mL. Noncompartmental parameters, obtained by utilizing
statistical moment theory, mean residence time (MRT), clearance (CL), and Vdss were calculated to be 2.8 d, 0.79 L/kg X d, and
2.2 L/kg, respectively.

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Title

Residual nematocidal effectiveness of ivermectin in cattle.

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