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Safety and clinical efficacy of tenvermectin, a novel antiparasitic 16-membered macrocyclic lactone antibiotics

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Abstract: Tenvermectin (TVM) is a novel 16-membered macrocyclic lactone antibiotics, which contains component TVM A and TVM B. However there is not any report on safety and clinical efficacy of TVM for developing as a potential drug. In order to understand the part of safety and clinical efficacy of TVM, we conducted the acute toxicity test, the standard bacterial reverse mutation (Ames) test and the clinical deworming test. In the acute toxicity studies, TVM, TVM A and ivermectin (IVM) were administrated once by oral gavage to mice and rats. Results showed that the oral LD_{50} values of TVM, TVM A and IVM in mice were 74.41, 106.95 and 53.06 mg/kg respectively. The oral LD_{50} values of TVM and TVM A in rats were determined to be 164.22 and 749.34 mg/kg respectively. TVM and IVM are moderately toxic substances, meanwhile the TVM A belongs to low toxic compounds, implying that the acute toxicity is highly related to the length of side chain of TVM at position C25. In the Ames test, results showed that TVM did not induce mutagenicity in *Salmonella typhimurium* TA97a, TA98, TA100, TA102 and TA1535 with and without metabolic activation system, speculating that the mutagenicity is probably not related to the side chain at position C25 of 16-membered macrocyclic lactone antibiotics. In the efficacy trail of TVM against swine nematodes, growing pigs natural infection of *Ascaris suum* and *Trichuris suis* were treated with a single subcutaneous injection 0.3 mg/kg b.w.. Results showed that TVM and IVM had excellent effect in expelling *Ascaris suum*, and TVM had potential efficacy against *Trichuris suis*, however IVM had no effect on *Trichuris suis*. This study suggests that the side chain of TVM at position C25 may have important biological functions, which is one of the key sites of the studies on structure-activity relationship of 16-membered macrocyclic lactone compounds. TVM is a new compound exhibited some advantages worthy of developing.

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