Inhibition of Bovine Herpesvirus 1 and Bovine Viral Diarrhea Virus Replication by Genistein—a Compound in Soybeans

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Introduction

Bovine herpesvirus type 1 (BHV-1, IBR), an alphaherpesvirus, and bovine viral diarrhea virus (BVDV), a pestivirus, are important cattle pathogens. Genistein, a naturally occurring flavonoid in soybeans, inhibits *in vitro* replication of herpes simplex virus 1, another alphaherpesvirus. Genistein has also been used to protect against a wide range of animal and human conditions including cancer, cardiovascular disease, loss of brain function, osteoporosis and menopausal symptoms. This makes genistein an excellent candidate for use as an anti-viral drug. Genistein was tested for its ability to inhibit the replication of BHV-1 and BVDV.

Materials and Methods

In vitro studies

The effect of a single high dose or sequential dosing of genistein on BHV-1 or BVDV replication was studied. MDBK cells were infected with 0.5 moi of BHV-1 or 1 moi of BVDV (NADL Type 1). The BHV-1 infected cells were treated at time 0 h with either a single dose of 50 μM genistein or with two 25 μM genistein doses, 12 hours apart. The virus was harvested at 24 hours. The BVDV-infected cells were treated at time 0 with a single dose of 25 μM of gentistein, or with 25 μM of gentistein every 24 hrs post infection for 72 hours (3 treatments).

In vivo studies

The metabolism of gentistein in ruminants was compared by feeding an isoflavone concentrate ingested from a bottle or pail. A second study is in progress to determine the effect of once- or twice-a-day dosing of Holstein calves infected with BHV-1.

Results and Conclusions

In vitro studies

The viral titer in cells sequentially treated with 25 μM genistein at 0 h and 12 hr post infection was 90-fold lower than in the untreated cells (1×10^5 $TCID_{50}$/ml versus $1 \times 10^{6.9}$ $TCID_{50}$/ml). This sequential double dosing of genistein was more effective than the single dose of 25 μM genistein in lowering the BHV-1 titer by 24 hr post infection (1×10^5 $TCID_{50}$/ml versus $1 \times 10^{5.8}$ $TCID_{50}$/ml). The effect of single dose of 50 μM genistein was comparable to the sequential double dosing of 25 μM genistein in inhibiting *in vitro* BHV-1 replication ($1 \times 10^{4.9}$ $TCID_{50}$/ml versus 1×10^5 $TCID_{50}$/ml). A single dose of genistein lowers the BVDV titer 100-fold, while the daily dosing of genistein lowers the BVDV titer 1000-fold.

In vivo studies

Calves that drank the gentistein treatment via bottle had higher levels of genistein in their blood compared to the animals who drank the treated milk from a pail. This was thought to be due to that ability of the suckling reflex to bypass the rumen and allow the genistein to be absorbed through the intestinal tract. The antiviral effects in the Holstein calves will be presented.

This research provides a potential use of soybean products in the milk of nursing dairy calves or feedlot rations as an antiviral agent in preventing BHV-1 and BVDV infections.