Viscum album use in pregnant rats: toxicity and safety evaluation

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Objective: The safety of intrauterine fetal exposure to VA was evaluated in a rat model with the objective of gathering further evidence for the safe use of therapeutic doses of VA in pregnant cancer patients.

Methods:

50 rats randomized, on day 0 of pregnancy, in 5 groups and weighted weekly on days 0, 7, 14 e 20 – daily application of 1 ml – medication *Viscum album extract (Iscador Qu 5mg)*

- Group 1: **controll group -** without medication
- Group 2: **stress group** – 1ml of FS 0,9% via SC
- Group 3: **therapeutic dose** (0,98ng de lectina/kg - 0,013mg of VA extract) - therapeutic group
- Group 4: **961 x** therapeutic dose (937ng de lectina/kg - 12,5 mg of VA extract) - high dose group
- Group 5: **1923 x** and 7,2% DL50 (1875ng de lectina/kg - 25 mg of VA extract) - very high dose group

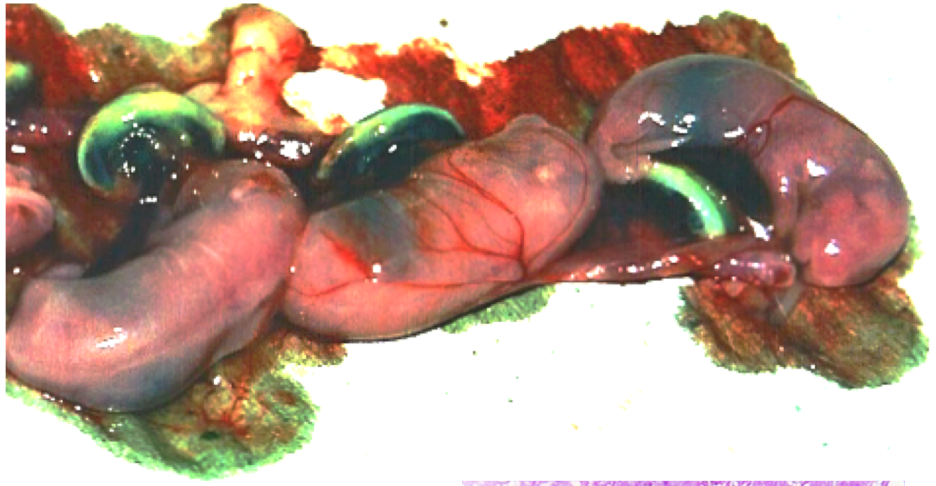
Morphological analysis of the fetuses (n=399) from 47 pregnant rats

- MACROSCOPY
  - Weight of pregnant rats (n= 50)
  - Weight of fetuses and placentas (n=399)
  - Modificated Wilson technique (n=383)
  - Evaluation of the heart *in situ* (n*=50)*
  - Weight of thymus (n=50)
- MICROSCOPY :
  - liver, kidney, heart, brain, placenta and thymus - immunhistochemistry of thymus to CD56, NK cell (n=10/each)
- RADIOLOGY (n=150)
  - Head, column, toracic chest, upper members

Results: There was found to be gain weight on placentas and fetuses in the therapeutic group and high dose group compared to stress group. Radiological evaluation of bones without changes. Histology of the placentas showed a greater inflammatory process in high dose group and very high dose group.

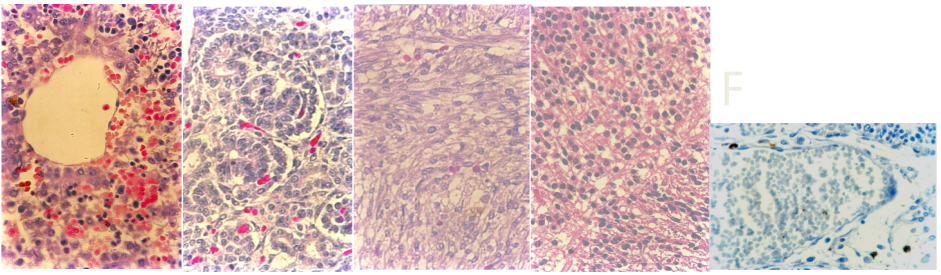
Results

Macroscopy of fetuses (N = 384)
211 males and 188 females; Malformation: only 1 fetus with fetal hydropsy.



Microscopy of fetuses

LIVER KIDNEY HEART. BRAIN THYMUS



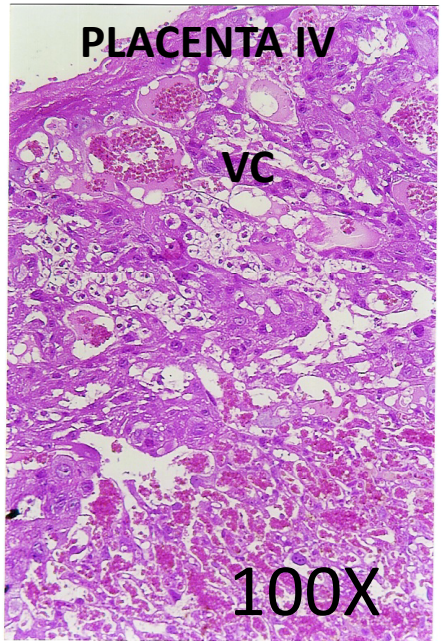
Microscopy of placenta

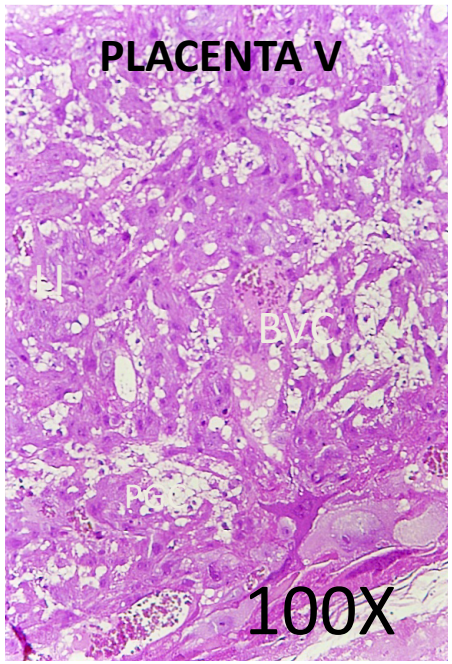
RELATED WITH INFLAMATORY PROCESS on groups IV and V:

- Thickening of external zone
- Improve of *sinus uterinus*
- Leukocyte infiltration
- Big vacuolizated cells
- Fibrin over the external surface

RELATED WITH IMMATURITY OF PLACENTA:

- Vesicular mononucleated cells
- Reduction of plasmodial giant cells





BVC = Big Vacuolized Cell

PGC = Plasmodial Giant Cell

VC=Vacuolizated Cell

F = FIBRIN

VMC = Vesicular Mononucleated Cell

LI = Leukocyte Infiltration

Conclusions

- There was a major gain of weight in pregnant rats, fetuses and placenta under subcutaneously daily therapeutic and high doses (961 times) of *Viscum album Qu 5 mg spezial,* when compared to the stress control group.
- The local inflammatory process on the rat placentas submitted to the daily high (961 times) and very high doses (1923 times) point to a dose-dependent pattern of VA affinity with the placenta.
- The absence of abortion, teratogenic, embryotoxic macroscopic signals in the fetuses, and also the absence of microscopic alterations in the hepatic, renal, cardiac, cerebral, and thymus fetal examined tissues allows us to consider VA as a safe drug, even administered in high and very high doses of 12.5 mg/kg and 25.0 mg/kg of body weight during the pregnancy of rats.

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