Prevention of Placental Insufficiency in Rats by Peat Humic Acids

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Placental insufficiency causes:

- Intrauterine hypoxia of fetuses
- Intrauterine growth restriction of fetuses
- Perinatal deaseses
- Increase of ante- and postnatal mortality

Correction and prophylaxy of placental insufficiency is aimed at the recovery of

- Uteroplacental blood circulation
- Pheological properties of blood
- Placental metabolism
- Structure and functions of cellular membranes

Research strategy

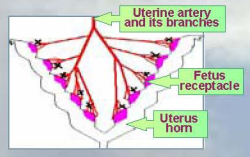
1st group – Control rats
10 females, 85 fetuses and placentas

2nd group – Rats with placental insufficiency (PI)
10 females, 84 fetuses and placentas

3rd group – Rats with HA-cured PI
10 females, 95 fetuses and placentas

Thirty pregnant rats of Wistar line were divided into 3 equal groups.

Experimental placental insufficiency was achieved by ligating of one third of preplacental arteries on the 15th day of pregnancy. The location of ligations is shown on the scheme (×).



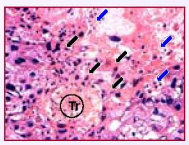
The rats with experimental placental insufficiency were cured with HA since the first day of pregnancy (the daily dose – 10 mg/kg per os). The initial 1% aqueous solution of HA with pH 8 was poured into a daily amount of drinking water and always fully consumed.

Methods:

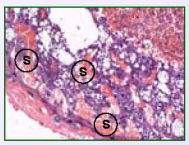
- Somatometry of fetuses
- Organometry of placentas
- Light microscopy
- Morphometry of placentas and placental beds
- Histochemistry (DNA, RNA, PAS)
- Immunohistochemistry (VEGF, WF)
- Electronic microscopy

Effects of humic acids

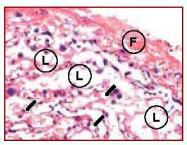
Prevention of uteroplacental blood circulation disorders



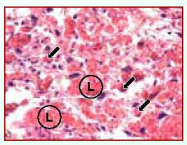
Basal part of placenta at PI. Thrombosis of blood maternal sine (Tr). Perifocal necrosis of trophoblastic cells (black arrows) with reactive leucocytic infiltration (blue arrows).



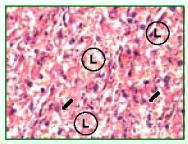
Basal part of HA-cured placenta. Blood maternal sines (S) are moderately dilated and sanguineous. No thrombuses in their lumen.



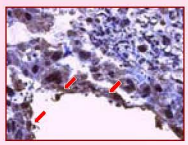
Marginal part of placental labyrinth at PI. Ischemic infarct: the dehematized empty maternal lacunas (L) and fetus capillaries (arrows), fibrinoid deposits in the chorial plate (F).



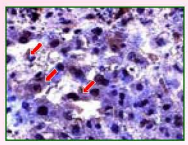
Central part of placental labyrinth at PI. Maternal lacunas (L) and fetus capillaries (arrows) with sharp hyperemia and erythrocyte stasis.



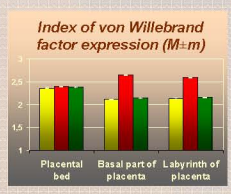
HA-cured placental labyrinth. Maternal lacunas (L) and fetus capillaries (arrows) are moderately dilated and sanguineous. No blood circulation disorders.



Basal part of placenta at PI. High expression of prothrombotic von Willebrand factor (strong brown staining in peri-vascular trophoblastic cells, red arrows).

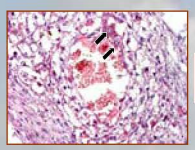


Basal part of HA-cured placenta. Low expression of prothrombotic von Willebrand factor in (weak brown staining in perivascular trophoblastic cells, red arrows).

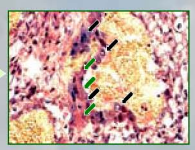


The decrease of index of von Willebrand factor expression in trophoblastic cells of basal part and labyrint of placenta is a convincing proof of homeostasis restoration in HA-cured rats

Stimulation of adaptation processes in placentas and placental beds

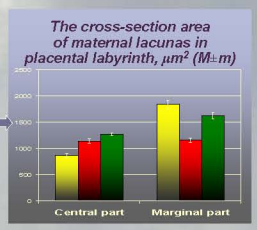


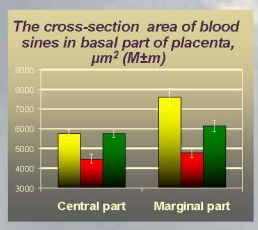
Placental bed at PI. Uncompleted gestational remodeling of uteroplacental artery: narrow lumen, thin wall with the lack of cytotrophoblastic cells (black arrows). Result – inadequate placental blood flow and hypoxia.

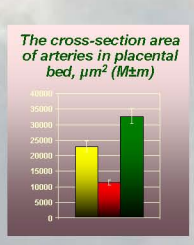


HA-cured placental bed. Complete gestational remodeling of utero-placental artery: the wall is replaced by cytotrophoblastic cells (black arrows) and fibrinoid (green arrows).

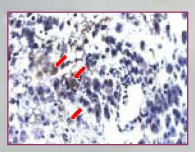
Adaptation processes developed in HA-cured placenta and placental bed are manifested by the dilating and moderate hyperemia of maternal lacunas of placental labyrinth, sines of basal part of placenta and arteries of placental bed. The cross-section area of the blood vessels is statistically higher than those in the case of untreated PI.



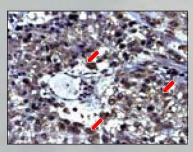




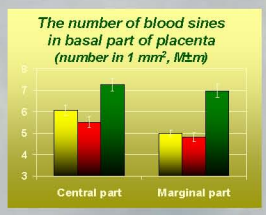
Stimulation of angiogenesis

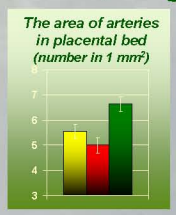


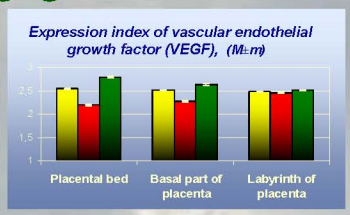
Placental bed at PI. Low VEGF expression index in decidual cells (red arrows).



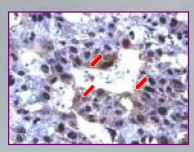
HA-cured placental bed. High VEGF expression index in decidual cells (red arrows) around the neogenic arteriole.



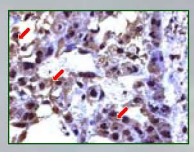




The number of blood vessels in basal part of placenta and placental bed is statistically increased in HA – cured group in comparison with PI- group and control. These changes are adaptive. Moreover, application of HA increases VEGF expression index in placental bed and basal part of placenta as compared with the rats with PI. Larger number of vessels and higher expression index of VEGF testify angiogenic action of HA.

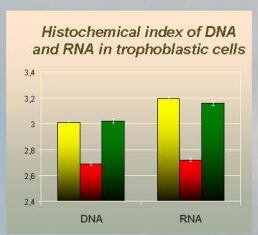


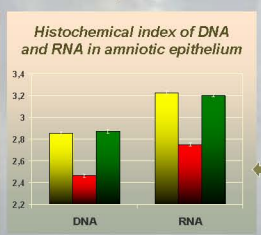
Basal part of placenta at PI. Low VEGF expression index in perivascular trophoblastic cells (red arrows).



Basal part of HA-cured placenta. High VEGF expression index in trophoblastic cells (red arrows).

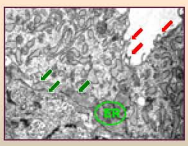
Activation of metabolic processes in placenta





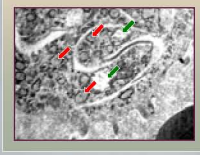
Humic acids stimulate metabolic processes as is seen from the increase of the histochemical index of DNA and RNA in trophoblastic cells and amniotic epithelium

Cytoprotective action on trophoblasts

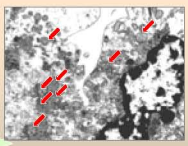


Placental labyrinth at PI. Ultrastructural damages of trophoblastic cells.

The number of microvillis at the surface of cells is reduced (red arrows). The rough endoplasmic reticulum (ER) is dilated and degranulated (green arrows).



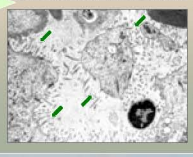
Homogenization of mito-chondrial matrix (red arrows) and destruction of cristas (green arrows) result from the damage of cytoplasmatic membranes.



Placental labyrinth of HA-cured rats. Ultrastructure of trophoblastic cells.

Hyperplasia of mitochondrions (red arrows) and microvillis on the cell surface (green arrows) gives the evidence of the development of adaptive processes at the subcellular level.

This is possibly connected with the protective effect of HA towards cell membranes.



CONCLUSIONS

Peat HA prevent placental insufficiency in rats induced by partial ligating of uteroplacental arteries

Application of peat HA results in the decrease of pre-implantation and post implantation mortality

Indices of embryomortality

Index	Control	PI	HA-cured PI
Pre-implantation mortality, %	10,6±1,5	11,8±2,2	4,8±1,6
Post-implantation mortality, %	6,9±3,0	14,4±1,7	6,0±1,7
Total embryonic mortality, %	17,0±2,2	24,4±2,9	10,5+2,4

Application of peat HA prevents uteroplacental blood circulation disorders and increases weight and length of fetuses (prophylaxy of intrauterine growth restrictions)