Polyoxometalates (POMs) cytotoxic and antiviral effect on human cells in vitro.

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Polyoxometalates (POMs) are stable metal-oxide inorganic compounds. Their structure and electronic properties can be lightly modified. They are one of the perspective products of nanotechnology in medicine and bioengineering, including antiviral and antitumor drug development.

Objective: to investigate POM's cytotoxic, antiviral, and immunomodulatory activity on cells culture.

Materials and methods: POMs samples ($H_3PW_{12}O_{40}$; $H_3PMo_{12}O_{40}$, $H_4SiW_{12}O_{40}$; $H_4SiMo_{12}O_{40}$, $H_3(PW_{12}O_{40})H_2O$) were investigated on human embryo fibroblast (HEF) cells, bone marrow cell from leukaemia patient (L-41), human lung carcinoma cells (A 549). Culture media with 10% fetal calf serum was used for cell culture. MTT test was applied for POM's cytotoxic studying. Growth-regulating activity was evaluated by proliferation index (PI). Influenza A virus (H3N2- A\Aichi\68) was used for investigation of POMs antiviral effect. Cells morphology was examined by light, electron (EM) and atomic-force microscope (AFM). POMs effect on immune system was measured by cytokine gene expression of IL-1β, IL-2, IL-4, IL-6, IL-8, IL-10, IL-12, IL-18, TNF-α, INF-α, INF-β, INF-γ, INF –λ RNA by RT-PCR method.

Results: POMs samples of interest showed different effect on cells structures. The most toxic effect had $H_4SiW_{12}O_{40}$; $H_4SiMo_{12}O_{40}$ samples. $H_3PW_{12}O_{40}$, $H_4SiW_{12}O_{40}$, $H_4SiMo_{12}O_{40}$ samples caused reduction of growth-regulating activity and destructive changes cells morphology. Hematoxylin-eosin staining method in light microscope (eye lens 10 x field lens 40) was used to investigate cells morphology. Dystrophic changes of cells structure with necrosis elements were detected after $H_3PW_{12}O_4$ exposure. Even complete failure of cells was found after $H_4SiW_{12}O_{40}$; $H_4SiMo_{12}O_{40}$ addition. These changes were proven by EM and AFM investigation. $H_3PMo_{12}O_{40}$ and $H_4SiW_{12}O_{40}$ samples showed antiviral effect: influenza A virus (H3N2- A\Aichi\68) infectious activity reduced by 2lg and more. POMs immunomodulatory activity showed that test samples promoted activation of INF-γ, IL-18, TNF-α, IL-1β, IL-8 gene transcription in HEF cells. These cytokines are responsible for cell and macrophage components of immune system. Polyoxometalates activated cytokine gene expression of INF I II III (INF-α/β, INF-γ, INF-λ).

Specimen	**HEF cells**
$H_3PW_{12}O_{40}$ **$H_3PMo_{12}O_{40}$** **$H_4SiW_{12}O_{40}$** **$H_4SiMo_{12}O_{40}$**	1) Antiviral immunity activation - activation of cell component of immune system Th1 (INF-γ, IL-18, TNF-α) and INF system (INF-β, INF-γ, INF-λ). 2) Activation of macrophage component of immune system (IL-1β, IL-8, TNF-α) – important in diseases, induced by intracellular causative agent (including viruses) and several neurological diseases (Parkinson disease, Alzheimer disease) 3) TNF-α gene expression activation, which is involved in antitumor immunity. It has cytotoxic and cytolytic effect on certain tumors. Also INF can cause direct apoptosis of tumor cells. 4) Depression of IL-10 transcription, which is important in atopic diseases, multiple sclerosis.

All samples activated TNF-α gene expression, which is involved in antitumor and antiviral immunity. It has cytotoxic and cytolytic effect on certain tumors. So, tested POM samples can be probably effective in tumor treatment.

Conclusion: POMs samples of interest showed different effect on cells structures and influenza H3N2 viral particles. POMs reduced viral load. These effects probably depended on their chemical structure. The most toxic effect had $H_4SiW_{12}O_{40}$; $H_4SiMo_{12}O_{40}$ samples. They caused destructive changes in morphology structures, seen in AFM. Obtained results in vitro demonstrated that POMs based drug development could be perspective in complex or monotherapy of viral infections, autoimmune, neurological and oncology diseases.