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INFLUENCE OF MISTLETOE EXTRACTS AND ITS COMPONENTS ON IN VITRO PHYSIOLOGY OF CANCER CELLS

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Abstract. The effect of various mistletoe preparations on cancer cells are well known [1]. We compared the induced cytotoxicity of ash and apple mistletoe extracts with common cytostatics such as Cisplatin, Paclitaxel and Doxorubicin. The effectiveness of these cancer therapeutics were depending on the concentration of the active agent, the cancer cell line and the presence of fetal calf serum (FCS) or mistletoe polysaccharides in the culture medium.

1. INTRODUCTION

The actual cancer therapy with mistletoe preparations is based on the tumor progression and the physical and mental health of the patient in general. The mistletoe therapy was established in 1922 by Rudolf Steiner and Ita Wegmann and is the most common in Germany today [3]. Mistletoe extracts contain a multitude of substances that have immunstimulatory and cytotoxic or anti-tumorigenic and antimetastatic effects, including visco-toxins and lectins (ML-I, ML-II, ML-III, VisalbCBA).

The mistletoes for the preparations derive from different trees. The final mistletoe extract is available as freshly pressed or fermented juice depending on the specific production process of the manufacturer. These different treatments result in a wide range of products.

The variety of the mistletoe preparations and the individual responsiveness of the patient to the mistletoe extract demand an effort to prognosticate the optimal therapy with the best individual medicament. In this sense we showed that the cytotoxicity of a distinct mistletoe extract is different regarding different cancer cell lines.

2. RESULTS

2.1. Effect of mistletoe extracts and cytostatics on the proliferation of the breast cancer cells MFM-223 and KPL-1

The extract of fresh apple mistletoe (Abnoba®Mali-2) and ash mistletoe (Abnoba® Fraxini-2) as well the chemotherapeutics Cisplatin, Paclitaxel and Doxorubicin were

added to the breast tumor cells MFM-223 and KPL-1 in decreasing concentrations from $10^{-1}$ to $10^{-4}$ mg·ml$^{-1}$. The toxic influence on the cells was controlled observing the cell proliferation (BrdU incorporation), the mitochondrial activity (MTT) and the cell viability (LDH). It was shown that mistletoe preparations have comparable, dose-de-pendent cytotoxic effect on cancer cells to common cytostatics. The viability of KPL-1 cells was diminished in the range of 60-80% when the concentration of chemothera-peutics was $10^{-3}$ mg·ml$^{-1}$. Lower doses from $10^{-2}$ to $10^{-4}$ mg·ml$^{-1}$ of Abnoba® Mali-2, Abnoba® Fraxini-2, Cisplatin and Doxorubicin had no influence on the cell prolifer-a-tion. Paclitaxel showed no effect on KPL-1. In contrast, the MFM-223 cell line reacted very sensitive to Paclitaxel in all concentrations tested, even at $10^{-4}$ mg·ml$^{-1}$ 80% of the cells were killed. $10^{-4}$ and $10^{-2}$ mg·ml$^{-1}$ Doxorubicin and the two mistletoe extracts lowered the viability of MFM-223 to 10-20%, whereas Cisplatin had a cytotoxic effect only at a concentration of 0.1 mg·ml$^{-1}$.

2.2. The influence of mistletoe lectins, viscotoxin and mistletoe polysaccharides on the growth of MOLT-4

The most powerful, cytotoxic agent of mistletoe extract was described to be the mistletoe lectin I (ML I) and viscotoxin [2]. We tested how isolated ML I and viscotoxin influenced the proliferation of MOLT-4 in the presence and absence of FCS. Finally, we supplemented the culture medium with mistletoe polysaccharides in combination with ML I or viscotoxin. We found, that viscotoxin only destroyed cells in high concentrations of 9 µg·ml$^{-1}$, whereas ML I stopped cell proliferation in the range of 2.5 ng·ml$^{-1}$ in the presence of FCS. In the culture medium without FCS, the ML I were diluted to 0.0025 ng·ml$^{-1}$ without any loss of toxicity compared to the highest dose of 250 ng·ml$^{-1}$. The addition of mistletoe polysaccharides (MS) reduced the toxic effect of ML I. However, viscotoxin seemed to stimulate the cell proliferation when mistletoe polysaccharides were present.

2.3. Mistletoe applications on primary breast cancer cells

Isolated breast cancer cells of three patients were cultured in the presence of three different mistletoe preparations: Abnoba Fraxini-2 (ash) corresponds to a fresh pressed extract, Isacodor M (apple) and Q (oak) were fermented mistletoe juices. All preparations showed cytotoxic effects in the highest concentrations of 01 mg·ml$^{-1}$: only 20% of the cells from patient 2 survived, the viability of the cells from patient 1 and 3 was reduced in the range of 40 to 50%. Cells of patient 1 reacted the most sensitive to Fraxi-ni-2, whereas cells of patient 3 were sensitive to Iscador M.

3. CONCLUSION

We conclude, that mistletoe extracts show comparable results to common cytostatics regarding the mitochondrial activity of tumor cells in vitro.