Cancer Therapy & Oncology
International Journal
ISSN: 2473-554X

Juniper Publishers
key to the Researchers

Research Article
Volume 27 Issue 1 - June 2024
DOI: 10.19080/CTOIJ.2024.25.556204

Cancer Ther Oncol Int J

Pilot Study: Evidence that High and Ultra-high Diluted Extracts of the anti-tumor active Mistletoe (*Viscum Album* L.) Plant Inhibit but may also Stimulate in Vitro Cell Proliferation of K562 Leukemia Cells

Razvan Rentea*, Mark Kamsler and Malory Mueller

Kolisko Institute for Anthroposophical Medicine, 1005 Richards Road, Hartland, Wisconsin, USA

Submission: May 23, 2024; **Published:** June 01, 2024

Corresponding author: Razvan Rentea MD, Kolisko Institute for Anthroposophical Medicine, 1005 Richards Road, Hartland, Wisconsin, 53029, USA, Email: ross.rentea@truebotanica.com

Abstract

Mistletoe extracts are widely used in Central Europe, as well as world-wide, as an adjuvant cancer therapy. In the laboratory, high doses of mistletoe extracts are largely considered to be uniformly inhibiting on cell proliferation in vitro. Some controversy has arisen however whether low doses of mistletoe extracts can be also stimulating and thus whether clinical low doses of mistletoe should be more cautiously administered in a clinical setting. We provide evidence that not only low but also highly and ultra-highly diluted extracts of mistletoe can both inhibit as well as stimulate in vitro cell proliferation.

Keywords: K562 cell line; Mistletoe; Viscum album; lectins; ultra-high dilutions; enantiodromic, Rudolf Steiner; L. Kolisko; IC50

Introduction

Mistletoe (*Viscum album* L.), a semi-parasitic plant that comes in several varieties depending on which host tree it grows on, has been shown in recent investigations both in vitro and in vivo to have potential in anti-tumor activity [1]. Most important to mistletoe's medicinal profile are its diverse array of bioactive compounds, principally mistletoe lectins, but also viscotoxins, flavonoids, and phytosterols [2,3]. Among the main mechanisms of action are cell cycle inhibition, generation of reactive oxygen species (ROS), disruption of mitochondrial function, activation of apoptotic pathways, and modulation of key signaling molecules involved in cell growth and survival [3] (Figure 1).

Mistletoe has also been found in clinical cancer studies to enhance the quality of life in patients through alleviating various symptoms (fatigue, sleep, exhaustion, nausea, vomiting, depression anxiety, pain) and to lower side effects of traditional treatments [4]. Based on well more than fifty in vitro studies on cell lines such as sarcoma, leukemia, melanoma, adenocarcinoma, etc., done with mistletoe lectin concentrations of 1.25ng/ml-1000ng/ml there seemed to be little doubt that in vitro experiments even at low concentrations the mistletoe extracts would be able to consistently inhibit cell proliferation [1-3,5].

However, some doubt was cast on this seemingly established result by a Gabius study [6] who found stimulation of tumor cells directly exposed to very low concentrations of mistletoe lectins. This stimulatory effect was seen at lectin levels of 50pg/ml x 10(5) cells in sarcoma and melanoma and hematologic lines. Several years after the Gabius study [6] another study by Kelter et al. [7] gave results that went into the direction of contradicting the concerns that mistletoe extracts with very low lectin concentrations would be stimulatory to cancer cell proliferation. They investigated 26 cell lines, including melanoma, sarcoma, CNS, etc., and found no stimulation at the level of 1.5 ng/ml up to 15mcg/ml total plant extract, corresponding to a lectin concentration of 0.0075-750 pg/ml.

In the present study we investigate the effect of mistletoe on the proliferation of K562 leukemia cells when the concentration of the mistletoe extract goes from low to ultra-high dilutions. This has not been done before.

Materials and Methods

Mistletoe (*Viscum album* L.) Extraction

The mother tincture (Ø) of the mistletoe growing on six different host trees was obtained through a proprietary method of extraction. The mistletoe was harvested from each host tree at two different opposing seasons (e.g., summer and winter) - the main rationale being that the summer viscum is richer in lectins and the winter viscum richer in viscotoxins. Thus, a combination of both seasons would provide a more full spectrum extract. After the separate extraction of each seasonal harvest, the summer harvest extraction was allowed to drip by gravity downwards into the centrifugally rotating extract from the winter season. The resultant final mother tincture was designated as Viscum and the name of the host it grew on as follows (Table 1).

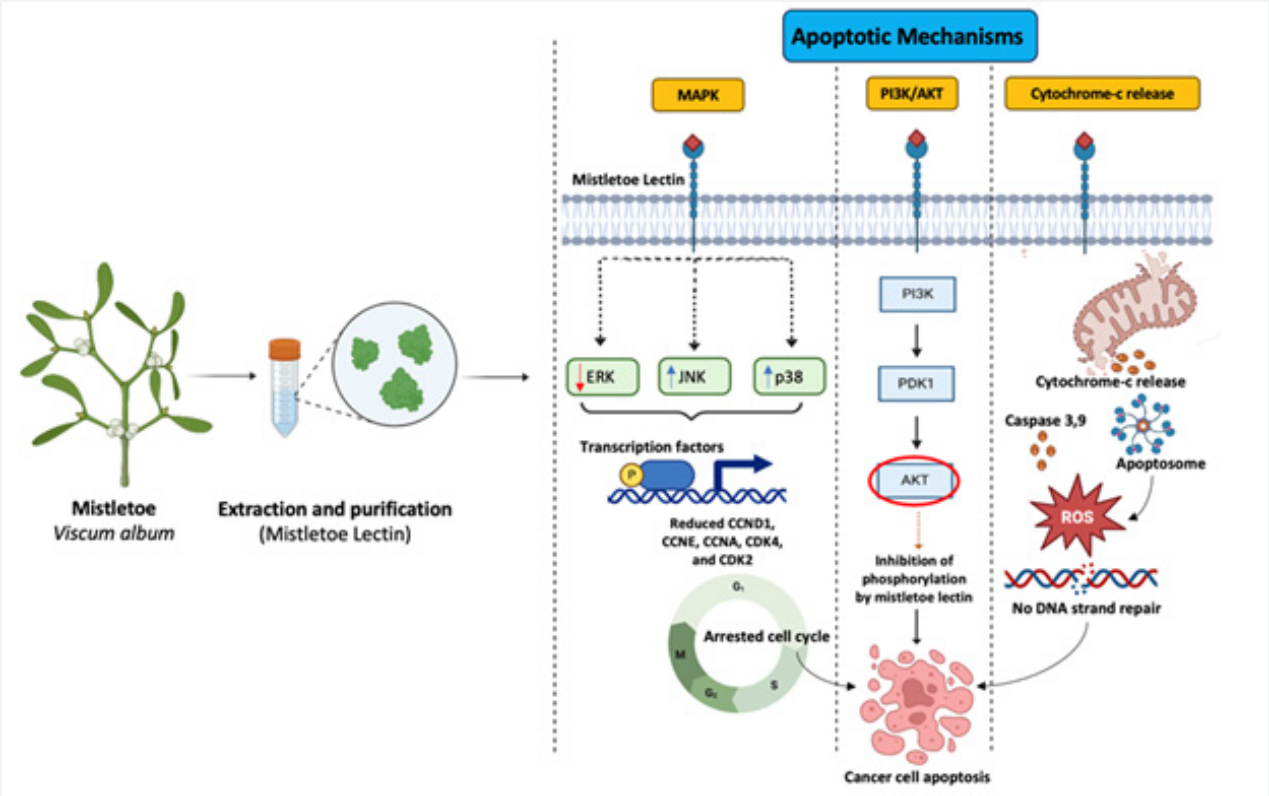

Figure 1: Summary of diverse apoptotic mechanisms of action of the mistletoe lectins, the most important bioactive Mistletoe component on cancer cells, including modulation via MAPK or PI3K/AKT pathways, or induction of cytochrome-c release. Dashed arrows denote omitted details within cascade pathways.

Table 1: Designation of the varieties of Mistletoe extracts depending on the Host Tree they grew on.

Grown on:	
Maple	*Viscum acer*
Hawthorn	*Viscum crataegus*
Poplar	*Viscum populus*
Robinia (pseudo0-acacia)	*Viscum robinia*
Willow	*Viscum salix*
linden	*Viscum tilia*

Preparing Dynamized "Dilutions"

The mother tincture was made from 20g dry plant material in 100cc diH_2O. The "dilutions" were prepared or so called "dynamized" in homeopathic style. The first "dilution" designated as D1, and was made by adding 1 part of mother tincture (Ø) to 9 parts of sterile diH2O. after that it was succussed (agitated) for 2 min and allowed to rest for 1 minute. One part of this D1 was added 9 parts of sterile diH_2O and again agitated as before. This was designated as D2. The procedure was followed until a D30 was obtained. The so called "dynamized"/agitated/then allowed to rest dilutions will be called in the following text only as "dilutions for ease of reading.

Cell Culture

The K562 human lymphoblast cell line (ATCC, CCL-243) was grown in 25cm^2 flasks, at 37°C, 5% CO_2, and the cell density was maintained between 1x10^5 and 1x10^6 cells/ml. The medium was IMDM (ATCC, 30-2005) supplemented with 10% Fetal Bovine

How to cite this article: Razvan R, Mark K, Malory M. Pilot Study: Evidence that High and Ultra-high Diluted Extracts of the anti-tumor active Mistletoe (Viscum Album L.) Plant Inhibit but may also Stimulate in Vitro Cell Proliferation of K562 Leukemia Cells. Canc Therapy & Oncol Int J. 2024; 27(1): 556204. DOI: 10.19080/CTOIJ.2024.27.556204

Serum (FBS; ATCC, 30-2020) and 1% penicillin streptomycin (ATCC, 30-2300). The Countess 3 was used to count cell inoculum and to determine viability.

Cancer cell and Mistletoe co-culturing

All assays were plated in white, 96-well plates (Costar, CLS3917) with a cell inoculum of 8 x 10^3. Each well contained 90 µl of cells plus 10 µl experimental dilution or "agitated" diH_2O (for the 0% and 100% controls), with four replicates per treatment or control. Plates were incubated at 37˚C and 5% CO2 for 72 hours. Cell growth was assessed using the Cell Titer Glo 2.0 cell viability assay (Promega, G9243), using 100 µl of reagent per well according to the manufacturer's instructions. The plate incubated at room temperature for 12 minutes before measuring the luminescence in a Bio Tek, Synergy LX plate reader. Cell growth was assessed for 0% control wells immediately, while sample and 100% control wells were assessed after 72 hours of growth.

IC 50 fitting and calculations

In our study, we employed the four-parameter logistic (4PL) model, which is a non-linear curve fitting model, to characterize sigmoidal dose-response curves of various viscum species, specifically for calculating half-maximum inhibitory concentrations (IC50s). The 4PL model is a mathematical function commonly utilized in pharmacological and biological assays to describe the relationship between the concentration of a compound (dose) and the response it elicits.

The IC50 values were calculated by the following equation:

$$c*[\left(\frac{(a-d)}{(50-d)}\right)-1]^{1/b}$$

where a is the minimum response, d is the maximum response, c is the middle point (c=(d-2)/2) and b is the slope in the semi-log axis, calculated by finding the location of the maximum difference in response and identifying the change in concentration at the maximum difference, with the below equation:

$$b=\frac{\log 10\left(y\left(indx\right)-\log 10\left(y\left(indx-1\right)\right)\right)}{\Delta x}$$

By fitting experimental data to the 4PL model, we were able to determine the IC50 values, which represent the concentration of the compound required to inhibit the response by 50%. This approach allows for the quantitative assessment of the potency of compounds and facilitates comparisons across different experimental conditions.

Statistics

Each experiment included 30 dilutions, in addition to the control samples. Each experiment was repeated in two plates at two locations (top/bottom) at two separate time intervals (Monday/Tuesday). Data from four plates was obtained, with 24 samples. The variation among and within the plates on various days and locations was examined using summary statistics and all samples were included in the analysis.

The raw data was summarized using descriptive statistics (mean, min, max, std, cv). The percentage of control was derived and summarized using descriptive statistics.

$$\%\,growth=\left(\frac{D_{value}-0\%\,control}{100\%\,control-0\%\,control}\right)X\,100\%$$

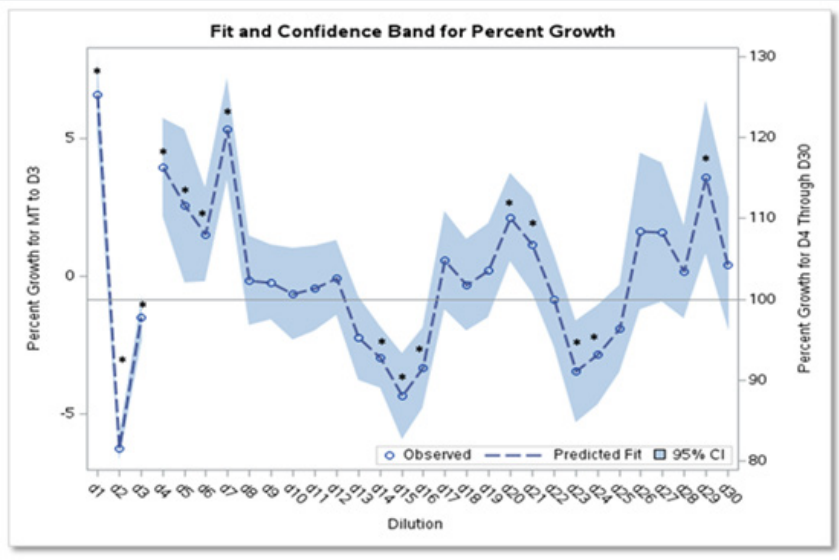

Figure 2: Viscum acer: graphical representations of the mean and corresponding 95% confidence intervals of percent of growth in comparison to the control. *indicates a stat. significant dilution.

How to cite this article: Razvan R, Mark K, Malory M. Pilot Study: Evidence that High and Ultra-high Diluted Extracts of the anti-tumor active Mistletoe (Viscum Album L.) Plant Inhibit but may also Stimulate in Vitro Cell Proliferation of K562 Leukemia Cells. Canc Therapy & Oncol Int J. 2024; 27(1): 556204. DOI: 10.19080/CTOIJ.2024.27.556204

This was calculated for each individual assessment. A value of 100 would indicate the growth was similar to the control, less than 100 would indicate the growth is less than the control and greater than 100 would indicate the growth is greater than control. The mean and the 95% confidence interval were computed and plotted. The mean percent growth and the 95% confidence interval (calculated as mean ±1.96 SE) is presented is graphically plotted below for various viscum species (Figure 2-7). The asterisks (*) denotes significantly different ($p<0.05$) from the control at the respective dilution (D) value.

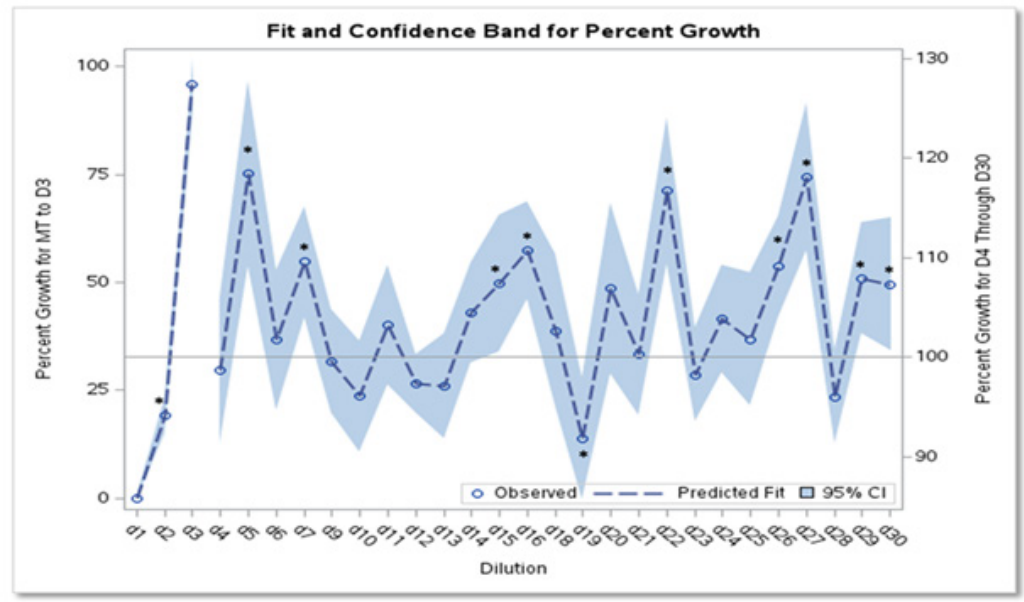

Figure 3: Viscum Crataegus: graphical representations of the mean and corresponding 95% confidence intervals of percent of growth in comparison to the control. *indicates a stat. significant dilution.

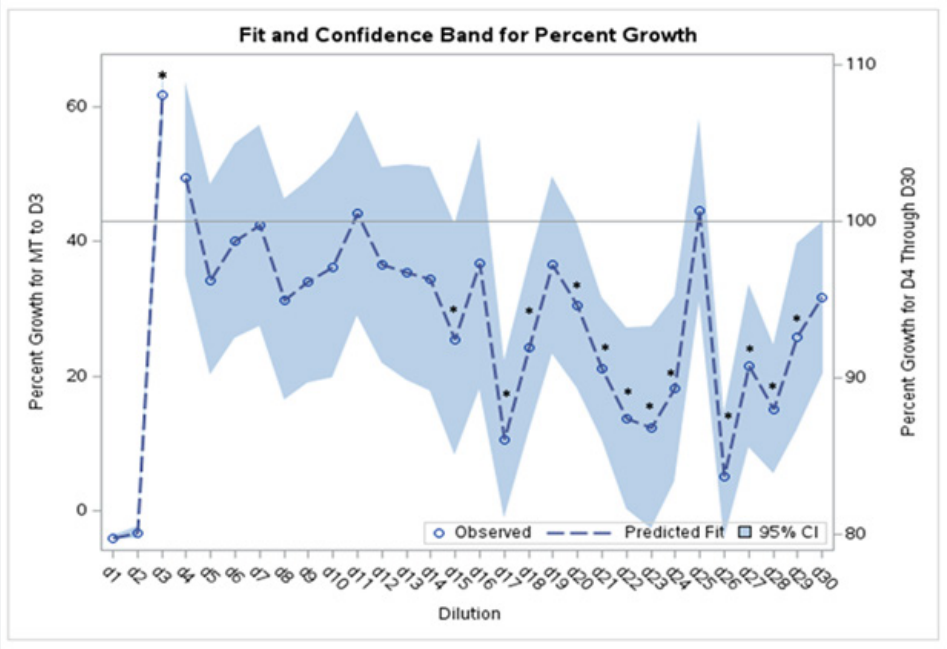

Figure 4: Viscum populus: graphical representations of the mean and corresponding 95% confidence intervals of percent of growth in comparison to the control. *indicates a stat. significant dilution.

How to cite this article: Razvan R, Mark K, Malory M. Pilot Study: Evidence that High and Ultra-high Diluted Extracts of the anti-tumor active Mistletoe (Viscum Album L.) Plant Inhibit but may also Stimulate in Vitro Cell Proliferation of K562 Leukemia Cells. Canc Therapy & Oncol Int J. 2024; 27(1): 556204. DOI: 10.19080/CTOIJ.2024.27.556204

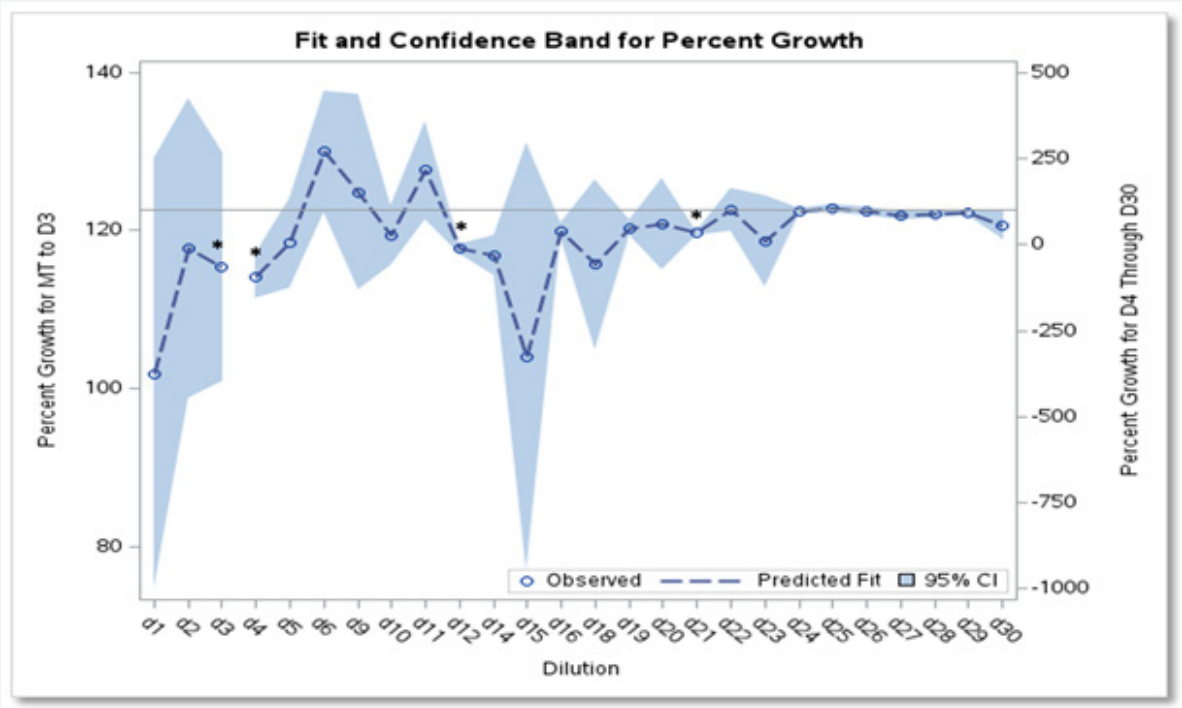

Figure 5: Viscum robinia: graphical representations of the mean and corresponding 95% confidence intervals of percent of growth in comparison to the control. *indicates a stat. significant dilution.

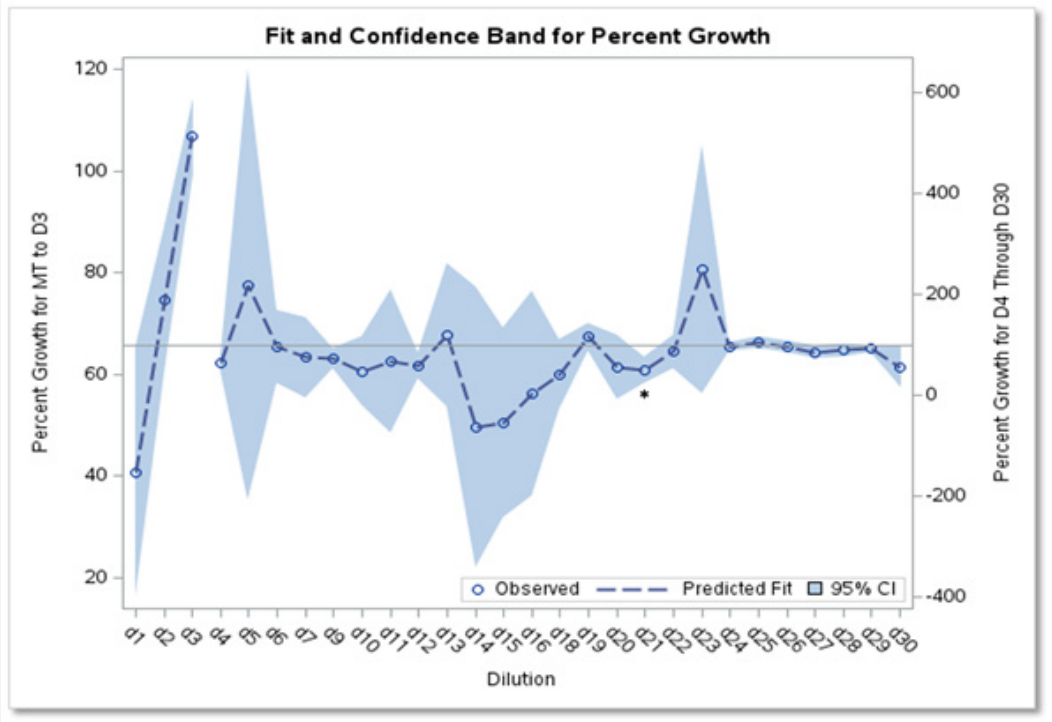

Figure 6: Viscum salix: graphical representations of the mean and corresponding 95% confidence intervals of percent of growth in comparison to the control. *indicates a stat. significant dilution.

How to cite this article: Razvan R, Mark K, Malory M. Pilot Study: Evidence that High and Ultra-high Diluted Extracts of the anti-tumor active Mistletoe (Viscum Album L.) Plant Inhibit but may also Stimulate in Vitro Cell Proliferation of K562 Leukemia Cells. Canc Therapy & Oncol Int J. 2024; 27(1): 556204. DOI: 10.19080/CTOIJ.2024.27.556204

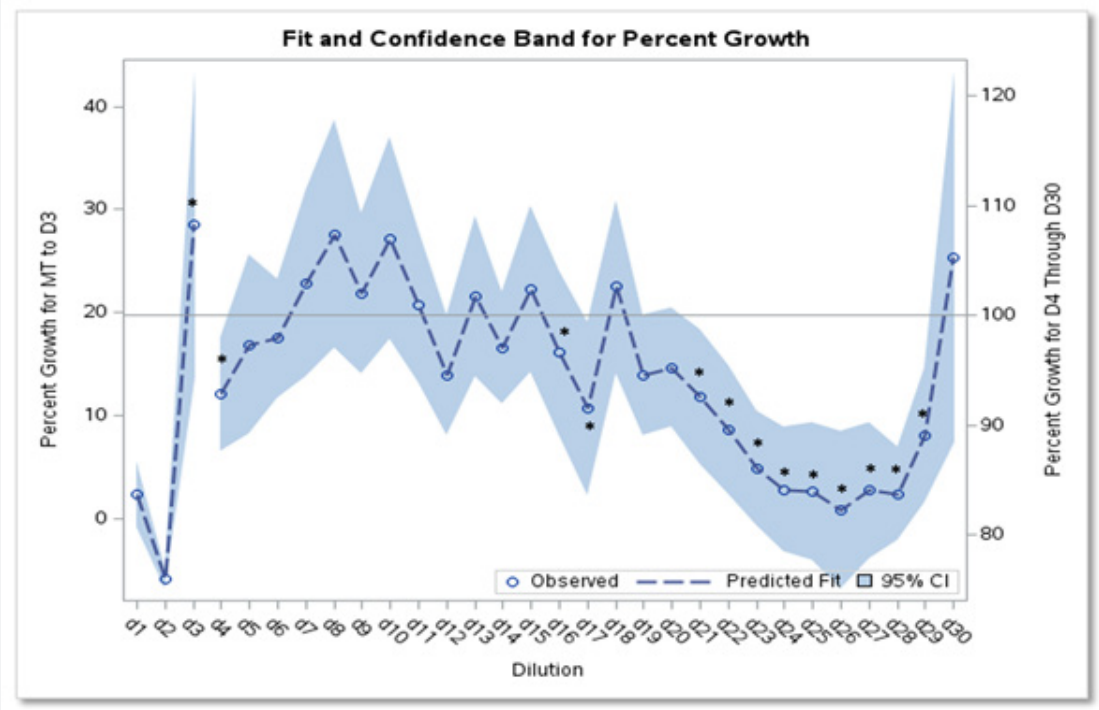

Figure 7: Viscum tilia: graphical representations of the mean and corresponding 95% confidence intervals of percent of growth in comparison to the control. *indicates a stat. significant dilution.

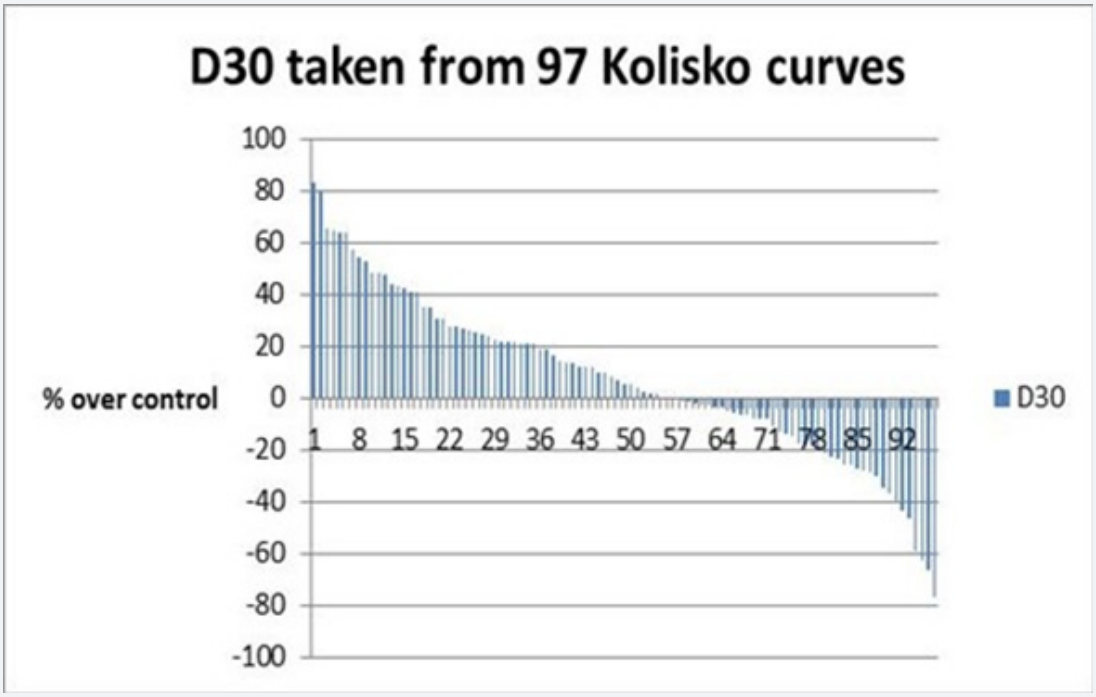

Figure 8: Comparison of the % growth of the wheat seeds over control in D30 dilutions from 97 Kolisko studies. In each study the wheat seeds were allowed to grow under the influence of varying substances. [15] The same dilution level of one substance can be inhibitory while of another it can be stimulating.

How to cite this article: Razvan R, Mark K, Malory M. Pilot Study: Evidence that High and Ultra-high Diluted Extracts of the anti-tumor active Mistletoe (Viscum Album L.) Plant Inhibit but may also Stimulate in Vitro Cell Proliferation of K562 Leukemia Cells. Canc Therapy & Oncol Int J. 2024; 27(1): 556204. DOI: 10.19080/CTOIJ.2024.27.556204

Results

IC50 Results (Table 2)

72-hour Incubation of K562 cells

This study was done in order to demonstrate that identical procedures done across columns in the plate are similar enough that no stat. significance was noted. Thus, when statistically significant results are obtained in the main experiment they can be relied upon not to be outliers (Table 3).

Inhibitory and Stimulating Dilutions of Six Different Mistletoe Varieties

Below, in Figure 2-7, are graphical representations of the mean and corresponding 95% confidence intervals of percent of growth in comparison to the control. *indicates a stat. significant dilution (Table 4).

Table 2. Anti-tumor efficacy of the various proprietary mistletoe species expressed as IC50 (inhibitory concentration) values in the K562 cell line.

Viscum species	Average IC 50 (mg/mL)
V. tilia	0.028
V. acer	0.119
V. salix	0.125
V. populus	0.206
V. crataegus	0.261
V. robinia	0.485

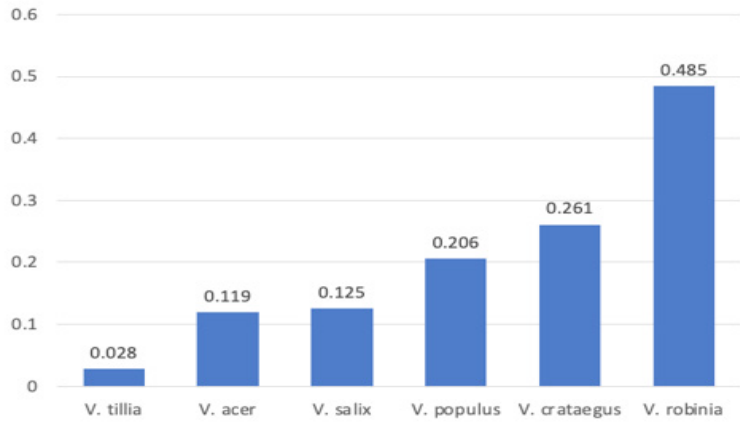

Table 3: 72-hour Incubation of K562 cells. Every cell value expressed in RLU's (Relative Light Units).

Summary						
Groups	**Count**	**Sum**	**Average**	**Variance**		
Column 1	16	10973559	685847.4	3.62E+09		
Column 2	16	11001719	687607.4	5.85E+09		
Column 3	16	10853759	678359.9	5.48E+09		
Column 4	16	10919663	682478.9	3.98E+09		
Column 5	16	10388505	649281.6	9.62E+09		
Column 6	16	10591150	661946.9	1.28E+09		
ANOVA						
Source of Variation	**SS**	**df**	**MS**	**F**	**P-value**	**F crit**
Between Groups	1.88E+10	5	3.75E+09	0.754442	0.585011	2.315689
Within Groups	4.48E+11	90	4.97E+09			
Total	4.66E+11	95				

How to cite this article: Razvan R, Mark K, Malory M. Pilot Study: Evidence that High and Ultra-high Diluted Extracts of the anti-tumor active Mistletoe (Viscum Album L.) Plant Inhibit but may also Stimulate in Vitro Cell Proliferation of K562 Leukemia Cells. Canc Therapy & Oncol Int J. 2024; 27(1): 556204. DOI: 10.19080/CTOIJ.2024.27.556204

Table 4: Summary of Inhibitory and Stimulating dilutions of the six tested mistletoe varieties. Values in RLU's (Relative light Units).

		Stimulating Dilutions				Inhibiting Dilutions		
		Mean	Lower	Upper		Mean	Lower	Upper
Viscum tilia		No Stimulating			D3	28.49475	13.55852	43.43098
					D4	92.80367	87.65771	97.94963
					D17	91.50569	83.59462	99.41676
					D21	92.61399	86.50317	98.72481
					D22	89.61848	83.7742	95.46277
					D23	86.10096	80.87877	91.32314
					D24	84.16205	78.50595	89.81814
					D25	83.95916	77.648	90.27031
					D26	82.28253	75.07409	89.49098
					D27	84.08231	77.89345	90.27117
					D28	83.74246	79.52197	87.96294
					D29	89.04232	82.86445	95.22018
Viscum acer	D4	116.2946	110.1884	122.4007	D1	6.616626	5.244497	7.988756
	D5	111.5433	102.0804	121.0062	D2	-6.25324	-6.7033	-5.80317
	D6	107.988	102.209	113.7671	D3	-1.50078	-2.30454	-0.69702
	D7	121.0016	114.6981	127.305	D14	92.79456	89.02543	96.5637
	D20	110.1268	104.6431	115.6105	D15	88.00642	82.6917	93.32113
	D21	106.7403	100.7623	112.7183	D16	91.49098	86.50877	96.4732
	D29	115.1076	105.6833	124.5319	D23	91.03657	84.76896	97.30418
					D24	93.15051	86.98251	99.31851
Viscum salix					D9	72.93868	53.05742	92.81995
					D12	58.71482	31.63799	85.79164
					D21	49.56778	22.55388	76.58168
					D30	55.52822	13.4073	97.64915
Viscum populus		No Stimulating			D3	61.80804	57.26987	66.34622
					D15	92.42697	85.04635	99.80758
					D17	86.10369	81.05753	91.14985
					D18	91.96998	86.57379	97.36617
					D20	94.65577	89.35339	99.95816
					D21	90.61	86.06638	95.15362
					D22	87.40374	81.6309	93.17658
					D23	86.81574	80.32703	93.30445
					D24	89.31103	83.42378	95.19829
					D26	83.71314	79.68477	87.74151
					D27	90.76979	85.60262	95.93697
					D28	87.99084	83.87264	92.10904
					D29	92.60948	86.64254	98.57642

How to cite this article: Razvan R, Mark K, Malory M. Pilot Study: Evidence that High and Ultra-high Diluted Extracts of the anti-tumor active Mistletoe (Viscum Album L.) Plant Inhibit but may also Stimulate in Vitro Cell Proliferation of K562 Leukemia Cells. Canc Therapy & Oncol Int J. 2024; 27(1): 556204. DOI: 10.19080/CTOIJ.2024.27.556204

Viscum crataegus	D5	118.4367	109.084	127.7894	D1	-0.0261	-0.44999	0.397799
	D7	109.5409	103.9043	115.1774	D2	19.09906	14.78804	23.41008
	D15	107.424	100.5562	114.2917	D19	91.80594	85.62442	97.98746
	D16	110.7575	105.8385	115.6766				
	D22	116.7511	109.3944	124.1078				
	D26	109.0468	103.9308	114.1629				
	D27	118.1297	110.6986	125.5608				
	D29	107.9226	102.3526	113.4926				
	D30	107.3184	100.6742	113.9625				
Viscum robinia	D3	115.4393	100.9423	129.9363	D4	-93.3986	-157.709	-29.0879
					D12	-12.6988	-27.197	1.799317
					D16	40.82179	16.357	65.28659
					D19	48.90181	24.41023	73.3934
					D21	33.45105	26.55958	40.34252

Discussion

We present evidence that the proprietary extract of the anti-tumor mistletoe (*Viscum album* L.) can have both inhibiting as well as stimulating effects on the proliferation of the K562 cell line at low as well as high and ultra-high dilution levels. All six mistletoe varieties tested demonstrated significant inhibitory activity but in three of the six varieties also stimulating effects could be observed. Thus, in three of the six varieties enantiodromic effects were observed i.e. effects in opposing directions depending on what concentration of mistletoe the cells were exposed to. These results are significant from multiple points of view. They align themselves with the increasingly well-established finding that contrary to the still wide spread pharmacological dose response model which predicts no effectiveness beyond a minimal low dose [8], a demonstrable activity will appear nevertheless after a certain "low dose" point [9].

Mechanistically, biological phenomena at low doses, such as low mother tincture concentrations, or going up to D23, are accepted, but when the dilutions go beyond the Avogadro number i.e. from a practical point of view no more physical mass of the original substance remain, meaning from D24 up, the existence of any biological activity is still being met with scepticism. This should not be the case since activity in the so called high homeopathic dilutions has been amply demonstrated [10-13].

Consequently, seeing both stimulating and inhibiting activity in range above the D24 dilution of the viscum acer and viscum Crataegus is highly notable. We are not the first to report the existence of such curves that contain both inhibiting and stimulating activity of dilutions of substances. First work in this direction was done in the 1920's when Rudolf Steiner and Lili Kolisko [14,15] demonstrated that serial dilutions of a multitude of substances resulted in semi-sinusoidal curve patterns containing these double switch effects of stimulating or inhibiting the mother tincture effect by various dilutions of the same substance. In later years this phenomenon was shown again and again f. ex. in an elegant study by Carmine [16].

In her pioneering work Kolisko demonstrated that each substance would have its own curve pattern. We have gathered the results of all 97 studies that she had done and compared the activity of the D30 dilution of each. Fig 8 below shows how different the activity level of each substance can be at the same D30 dilution- going from stimulating to inhibitory or to activity no different than control. These findings are especially significant in the work with the mistletoe extracts which are used clinically in anti-cancer therapy. We have found here that stimulation can occur both at low dilutions (D4, D5, D6, D7) as well as at high and ultra-high (D26-D30). This stimulatory occurrence makes the necessity for future extensive in vitro and pre-clinical testing with each mistletoe variety on each tumor cell line (here on leukemic cells) a requirement.

L. Kolisko [15] had envisioned that in the future doctors would have a detailed knowledge of the concrete dilution curve of each substance before being used clinically to ensure its appropriate and most effective use. This has not happened yet to today, not in the laboratory in vitro, or ex vivo, and not in clinical studies. Much more work is awaiting to be done.

Authors Participation

i. R Rentea MD - designed or wrote the article; also participated in the extraction of the mistletoe material.

ii. M Mueller M. Sc - executed the experimental data and wrote the Materials & Methods section.

How to cite this article: Razvan R, Mark K, Malory M. Pilot Study: Evidence that High and Ultra-high Diluted Extracts of the anti-tumor active Mistletoe (Viscum Album L.) Plant Inhibit but may also Stimulate in Vitro Cell Proliferation of K562 Leukemia Cells. Canc Therapy & Oncol Int J. 2024; 27(1): 556204. DOI: 10.19080/CTOIJ.2024.27.556204

iii. M Kamsler MD - participated in the extraction of mistletoe material.

Acknowledgement

i. Our thanks to Ashley Pajak for help with the statistical calculations and Nourhan Shalaby PhD for help with the calculations of the IC50 values and the mechanisms of inhibition chart.

ii. Our thanks to Peter Goedings PhD for invaluable ideas toward the making of the mother tinctures of mistletoe.

iii. Our thanks to Cosmin Borcea for the harvesting of the mistletoe.

Conflict of Interest

The authors report no conflict of interest.

References

1. Szurpnicka A, Kowalczuk A Szterk A (2020) Biological activity of mistletoe: in vitro and in vivo studies and mechanisms of action. Arch Pharma Res 43(6): 593-629.
2. Burger A, Mengs U, Schueler JB, Fiebig HH (2001) Anti proliferative activity of an aqueous mistletoe extraction on human tumor cell lines and xenografts in vitro. Arzneimittelforschung/Drug Res 51(9): 748-757.
3. Park YY, Do YR, Jang BC (2012) Apoptosis of K562 leukemia cells by Abnobaviscum F, a European mistletoe extract. Oncology Rep 28(6): 2227-2232.
4. Kienle GS, Kiene H (2024) Influence of Viscum album L. (European Mistletoe) Extracts on Quality of Life in cancer patients: A Systematic Review of controlled Clinical Studies. Rev Articles Integr Cancer Ther 9(2): 142-157.
5. Twardziok M, Kleinsimon S, Rolff J, Jaeger S, Eggert A, et al. (2016) Multiple Active Compounds from Viscum album L. Synergistically Converge to Promote Apoptosis in Ewing Sarcoma. Plos One 11(9): e0159749.
6. Gabius H, Darro F, Remmelink M, Andre S, Kopitz J, et al. (2001) Evidence for Stimulation of Tumor Proliferation in Cell Lines and histotypic Cultures by clinically relevant low doses of the Galctoside-Binding mistletoe Lectin, A Component of proprietary Extracts. Cancer Investigation 19(2): 114-126.
7. Kelter G, Flebig HH (2006) Absence of Tumor Growth Stimulation in a panel of 26 tumor Cell Lines by Mistletoe (viscum album L.) Iscador Extrracts in vitro," Arzneim.-Forschung/Drug Res 56(6a): 435-440.
8. Salahudeen MS, Nishtala P (2017) An overview of pharmacodynamic modelling, ligand-binding approach and its application in clinical practice. Saudi Pharma J 25(2): 165-175.
9. Calabrese EJ (2006) The Failure of Dose-response Models to Predict low Dose Effects: A Major Challenge to Biomedical, toxicological and Medical Research. Biogerontology 7(2): 119-122.
10. Dei A, Bernardini S (2015) Hormetic Effects of Extremely Diluted Solutions on Gene Expression. Homeopathy 104(2): 116-122.
11. Vallance A (1998) Can Biological Activity be maintained at Ultr-High Dilution? An Overview of Homeopathy, Evidence and Bayesia Philosophy. J Alternative Complementary Med 4(1): 49-76.
12. Witt CM, Bluth M, Albrecht H, Weisshuhn T, Baumgartner S (2007) The invitro evidence for an effect of high homeopathic potencies-A systematic review of the literature. Complementary Therapiesin Med 15(2): 128-138.
13. Sunila ES, Kuttan R, Preethi K, Kuttan G (2009) Dynamized Preparations in Cell Cultures. Complementary and Alternative Med 6(2): 257-263.
14. Steiner R (1999) Introducing anthroposophical Medicine, hudson, NY, USA: Anthroposophic Press 170-72.
15. Kolisko L (1959) Physiologischer und physikalischer Nachweis der Wirksamkeit kleinster Entitaeten, Stuttgart: Arbeitsgemeinschaft anthroposophischer Aerzte.
16. Carmine TC (1997) Effects of High Potencies of Tumor Necrosing Factor alpha on H_2O_2 production in cultured neuroblastoma Cells by enhanced luminol-dependent chemifluorscence (ECL) A positive system for investigating the biological significance of homeopathic high potencies. British Homeopathic J 86: 67-72.

DOI: 10.19080/CTOIJ.2024.27.556204

How to cite this article: Razvan R, Mark K, Malory M. Pilot Study: Evidence that High and Ultra-high Diluted Extracts of the anti-tumor active Mistletoe (Viscum Album L.) Plant Inhibit but may also Stimulate in Vitro Cell Proliferation of K562 Leukemia Cells. Canc Therapy & Oncol Int J. 2024; 27(1): 556204. DOI: 10.19080/CTOIJ.2024.27.556204