Report 2025

Society for Cancer Research
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Society for Cancer Research
Hiscia Research Institute

Society for Cancer Research
The primary aims of the Society for Cancer Research are assuring, optimizing and developing holistic cancer therapies on the foundations of anthroposophic medicine and pharmacy.

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Editorial

Dear members, friends and supporters of the Society for Cancer Research

The present annual report does once again provide an insight into our research work, which is as rich and multifaceted as the anthroposophic and integrative oncology to which we are committed.

Our botanical department looks back on over 50 years of experience in mistletoe cultivation. In his article, Hartmut Ramm describes how – based on such wealth of experience – we must nevertheless remain flexible, as climate change is confronting our mistletoe population with unprecedented challenges. With more than 14 hectares of our own land and well over 600 mistletoe-bearing oak trees, we take responsibility: for security of supply, for the quality of the mistletoe plant, and for a sustainable relationship with nature.

Identifying the constituents of mistletoe has been and remains a scientific challenge. Konrad Urech and Jakob Maier report on the results of an international collaboration with the University of Rio de Janeiro: using state-of-the-art analytical methods, over 100 different chemical compounds have been identified in the fat-soluble mistletoe resin. These findings form the fundamental basis for the development of new preparations – and remind us of how much lies hidden within this seemingly simple plant.

Our scientific focus extends beyond mistletoe. Devika Shah presents research on *Helleborus foetidus* – another winter-flowering plant with remarkable biological properties and potential for the integrative cancer therapy. Johannes Fahrentrapp and Maria Olga Kokornaczyk, in turn, demonstrate in their methodological study that homeopathic multi-component mixtures can be qualitatively characterised using the drop evaporation method – and that the whole is indeed greater than the sum of its parts.

Finally, we are delighted to give a personal voice a platform in this report: Ulrike Weissenstein, Head of our Tumour

Biology and Pharmacology Research Group, looks back in an interview on 20 years of research at the Society for Cancer Research. Her journey – from basic research through mentoring young scientists to clinically relevant questions – epitomises the spirit that underpins our work: curious, meticulous, and always people-centred.

We would like to thank you warmly for your loyalty and trust. The research you make possible contributes to a form of medicine which aims to support people – in the broadest sense.

Prof. Stephan Baumgartner

Head of Research and Development

Mistletoe Cultivation in the Face of Climate Change

DR. HARTMUT RAMM

50 years of practical research form the basis for successful mistletoe cultivation, ensure the supply of rare mistletoe and help to overcome new challenges posed by climate change.

The Society for Cancer Research is a pioneer in the field of pharmaceutical mistletoe cultivation. The project was launched in 1976 to secure the long-term supply of mistletoe from rare mother trees. The botanical department has researched the factors for sustainable mistletoe growth.

It all began with the discovery that mistletoe-bearing elms and oaks are genetically predisposed to host mistletoe and that this trait can be passed on to their offspring: most reliably vegetatively via grafted scions – more sustainably, but more labour-intensive, generatively via wild seeds. We now rely on seeds from our own oak and elm tree population, whose predisposition for hosting mistletoe has been enhanced through cross-pollination.

Mistletoe cultivation is a long-term project and relies on having our own land for the mistletoe trees. Initially, the main criterion was the purchase price; later, travel time and size of the land became important. Soon, however, soil quality also came into focus: for oaks prefer acidic and iron-rich soils! Today, the Society owns more than 14 hectares of land for mistletoe cultivation, on which well over 600 mistletoe-bearing oaks grow.

As soon as the trees are tall enough, we test their mistletoe potential. Successful mistletoe sowing depends on the seed, the quality of which we ensure through early preparation and careful overwintering of large mistletoe seeds (Fig. 1). Suitable weather conditions are necessary for sowing: Mistletoe seeds sown too early are often eaten by blue tits during late frosts, whilst snow or rain showers make it difficult for the seeds to attach. If sowing takes place too late and the seed stems have stretched too far, the mistletoe embryos can no longer attach to the bark. The optimal period is from early March to mid-April.

During testing, the first mistletoe seeds are sown on the trunk, although this impairs the growth of young trees. For harvesting, mistletoe seeds are later preferably sown in the upper tree canopy. This is always done on one-year-old branches, whose thin bark allows the mistletoe embryos to grow through easily. There, the active cambium also promotes the embedding of the mistletoe haustorium and its connection to the tree.

Regular mowing between and beneath the trees keeps slugs away, which eat young

Fig. 1: Every winter, we prepare up to 40,000 mistletoe seeds by separating them from their fruit skins (left) and leaving them to dry in Petri dishes (right), so that they can be stored in a cool, light-filled place until sowing.

mistletoe, and disturbs voles that settle under the protection of the tree canopy.

The tree species influences mistletoe growth: on elm and apple trees, mistletoe bushes reach harvest maturity faster than on oak, pine and fir. However, the cultivation of the mother trees must also be considered in cultivation planning. We therefore estimate that it takes 10–12 years for elm mistletoe, 20–25 years for oak mistletoe and 30–40 years for fir mistletoe before sufficient quantities can be harvested.

For us, harvesting mistletoe means also mistletoe care. When picking berries and working on the same mistletoe bush for a long time, we can intervene specifically where too many branches are forming, whose berries remain small and unripe. Like fruit trees, mistletoe bushes also benefit from targeted thinning.

The more mistletoe berries a site offers in winter, the more attractive it becomes to mistletoe-eating birds, which can help us with mistletoe propagation. This applies in particular to blackcaps, which often carefully stick mistletoe seeds onto thin twigs of the same tree.

Despite obstacles such as resistance in oak trees and the decline of elm trees, we are now able to meet the demand for their mistletoe from our own stocks

Fig. 2: This mistletoe-bearing oak tree grew from an acorn that was sown directly in the field in 1990.

(Fig. 2). Compared to wild harvesting, which sometimes requires time-consuming permits, this makes it considerably easier to plan the number of trees and amount of mistletoe needed for future harvests. Furthermore, having our own land allows us to specifically enhance the quality of the mistletoe, for example by applying biodynamic preparations.

Tree diseases such as Dutch elm disease can wipe out mistletoe populations in a short space of time. By continuously propagating young mistletoe-bearing elms, we are helping to boost the resilience of this endangered tree species. New challenges are emerging due to climate change. As conifers are particularly affected, we now also grow mistletoe on our own fir trees.

Prolonged drought in spring, when trees and mistletoe grow most vigorously, inhibits their growth and can lead to their death. On several occasions, such sudden droughts have already required targeted supplementary watering. To be prepared for any emergency, we are setting up mobile water storage facilities and are optimising our irrigation logistics. Backed by 50 years of botanical research and practical experience, we are confident that we are also up to the task of meeting these new challenges. ■

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The Fat-Soluble Substance in Mistletoe – a Spectrum of over 100 Chemical Compounds

DR. KONRAD URECH, DR. JAKOB MAIER

The Society for Cancer Research, in collaboration with a working group at the University of Rio de Janeiro, commissioned an analysis of the so-called mistletoe resin to determine its constituents.

Rudolf Steiner had already drawn attention to the significance of the fat-soluble substance in mistletoe by proposing the processing of this 'glue-like substance' into a mistletoe preparation for the treatment of cancer patients. We discovered that this fat-soluble 'glue-like substance' contains a high proportion of steroid-related compounds, namely pentacyclic triterpenes, which have long been known for their anti-tumour effects. Thus, work on the fat-soluble substance – historically known as 'mistletoe glue' – became a focal point of research in the department of pharmaceutical development of the Society for Cancer Research.

This work has resulted in the production of a resinous CO_2 extract (hereinafter referred to as 'mistletoe resin') and the development of an initial preparation derived from it: a mistletoe resin cream for the topical treatment of 'white' skin cancer. It has already received approval from the Swiss Agency for Therapeutic Products (Swissmedic) as an anthroposophical preparation for individual therapy and has found its way into medical practice. An initial case series study indicates the efficacy of this preparation (Königsberger et al. 2024).

Our next step is aimed at producing an injectable mistletoe resin preparation. This necessitated a more in-depth investigation of the composition of this mistletoe resin. Thanks to collaboration with the Metabolomics Laboratory and the Faculty of Pharmacy at the University of Rio de Janeiro (Brazil), results are now available on the diversity of chemical compounds in this mistletoe resin (de Souza et al. 2025). Using modern analytical methods (mass spectrometry coupled with gas and

liquid chromatographic separation of the substances), this research group was able to record data on 103 different chemical compounds. These include the six pentacyclic triterpenes, which we had already identified as pharmacologically active compounds in 2005 (Urech et al. 2005) in the mechanically extracted 'mistletoe glue'. A newly discovered tetracyclic triterpene and a diterpene compound have now been added to this group of mistletoe terpenes. This group of mistletoe terpenes, together with two phytosterols, formed the main component of the mistletoe resin. Various fatty acids, flavonoids, alcohol compounds, hydrocarbons, amino acids and other chemical compounds were also identified. Among the more than 100 substances, the presence of vitamin E, a fat-soluble substance with strong antioxidant properties, is worth noting.

We therefore acknowledge mistletoe resin as a highly complex mixture of multiple substances with a clear emphasis on terpenes. We intend to investigate this potential of multiple effects further and make it available in new preparations. ■

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Fig. 1: Helleborus foetidus – flowering plants in February.

Discovery of New Biologically Active Substances in Helleborus Foetidus

DEVIKA SHAH

The winter-flowering plant setterwort (*Helleborus foetidus*) holds great potential in the fight against cancer due to certain compounds it contains (bufadienolides).

In addition to mistletoe, there are other winter-flowering plants that can be used in anthroposophic medicine for integrative cancer therapy. One of these is the setterwort (*Helleborus foetidus* L.) (Fig. 1), which Rudolf Steiner already had recommended during a medical consultation for the treatment of cancer patients.

From an anthroposophical perspective, a distinctive feature of winter-flowering plants is that their warm, metabolic flowering process happens during the deep, rigid cold of winter; which stands in contrast to the cancer process, where a cold process spreads within a warm, metabolically active area of the organism. Thus, this counter-tendency of winter-flowering plants represents an antithesis to neoplastic diseases.

In addition to various anthroposophical-Goethean studies on the morphological development of *H. foetidus,* biological investigations and analyses of constituents were carried out on various *H. foetidus* extracts in collaboration with the University of Applied Sciences of Northwest Switzerland and the Department of Pharmaceutical Sciences at the University of Basel.

The *H. foetidus* extracts were derived from different parts of the plant (leaves, stems, flowers, etc.) and harvested at different times. Initially, various aqueous *H. foetidus* extracts were examined for their biological activities. A significant cytotoxic (cell-killing) effect of the various extracts on breast cancer cells (MCF-7 cells) was observed. In a subsequent step, the *H. foetidus* extracts were fractionated using a chemical analysis method (HPLC) and their anti-cancer activity was assessed in cell cultures. It became clear that the strong cytotoxic effect of the fractions could be attributed to the bufadienolides they contained. Bufadienolides are cardiotonic substances found only in a few plant genera (e.g. *Helleborus*, *Bryophyllum*, *Drimia*) and also in the skin of toads (*Bufo*).

As part of two master's theses at the University of Basel, comprehensive chemical analyses of the bufadienolides in our *H. foetidus* plants were carried out. In the process, 18 bufadienolides were isolated and characterised. These included eight bufadienolide glycosides (bufadienolides with a sugar molecule) and ten bufadienolide aglycones (bufadienolides with-

out a sugar molecule). Nine of these 18 bufadienolides were described for the first time in this study, and a further one was isolated from a plant for the first time. All these new substances, which were found first in *Helleborus foetidus*, were given names linking them to the plant: *Hellefoetin A, B, C* etc. for the bufadienolide aglycones and *Hellefoetinoside A, B, C* for the bufadienolide glycosides.

In a further step, the effects of these 18 different bufadienolides were measured individually on the aforementioned breast cancer cells, and it was found that these molecules exhibited very different cytotoxic effects: some bufadienolides are highly cytotoxic even in small quantities, whilst others showed only low cytotoxicity. Interestingly, it has been shown that all highly cytotoxic bufadienolides share one common chemical feature: an aldehyde group at a specific position in the bufadienolide molecule.

The diversity of bufadienolides in *H. foetidus,* as well as their potent biological effects, reflects the significance of these substances in this fascinating plant. As already mentioned, bufadienolides are also abundant in the skin glands of toads. Significantly, the toad was recommended by R. Steiner as a further remedy for cancer. In Traditional Chinese Medicine, too, such a remedy has long been used for tumours (e.g. the toad-based remedy HuaChanSu).

It is with great enthusiasm and curiosity that we will continue our research into this remarkable plant, *Helleborus foetidus*, with the aim of then incorporating the insights gained into the further development of an innovative preparation. ■

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Using the Droplet Evaporation Method to Investigate the Properties of Multi-Component Mixtures

DR. JOHANNES FAHRENTRAPP, DR. MARIA OLGA KOKORNACZYK

In this study, diluted and potentised multi-component mixtures of plant extracts and salt solutions were investigated using the droplet evaporation method. The mixtures revealed new and richer structures which cannot be derived from the structures of their individual components. This provides qualitative confirmation that a mixture can be more than the sum of its parts and that the droplet evaporation method has potential for characterising multi-component mixtures.

Naturopathic medicines are often composed of several ingredients. In addition to plant extracts, which, unlike synthetically produced substances, consist of a multitude of different molecules, naturopathic preparations may also contain salt solutions and other active ingredients. This is why they are referred to as 'multicomponent mixtures'. Describing the effect and quality of such molecular mixtures is difficult. As a rule, only the effects of the active substances contained within them are described and researched; however, the 'whole' of such multi-component extracts is rarely examined. Here, we describe a qualitative study in which we compared plant extracts on their own, salt solutions on their own, and mixtures of these two components.

Therefore, we employed the so-called droplet evaporation method. In this method, drops of the liquid under investigation are allowed to dry on glass slides. The crystalline patterns formed can then be observed, analysed and compared under a microscope. Such patterns, which form in dried drops, have previously enabled the qualitative characterisation of homeopathic preparations of various substances. The aim of the study described here was to examine mixtures of various plant extracts and salt solutions in D2 and

Plant extracts	Dyer's rocket (*Baptisia*)
	Black cohosh (*Cimicifuga*)
	Lady's slipper (*Cypripedium*)
	Coneflower (*Echinacea*)
	Horsetail (*Equisetum*)
	Passion flower (*Passiflora*)
	Stinging nettle (*Urtica*)
Salt solutions	Copper chloride
	Copper sulphate
	Potassium nitrate
	Sodium sulphate
	Sodium chloride

Table 1: The plant extracts and salt solutions studied.

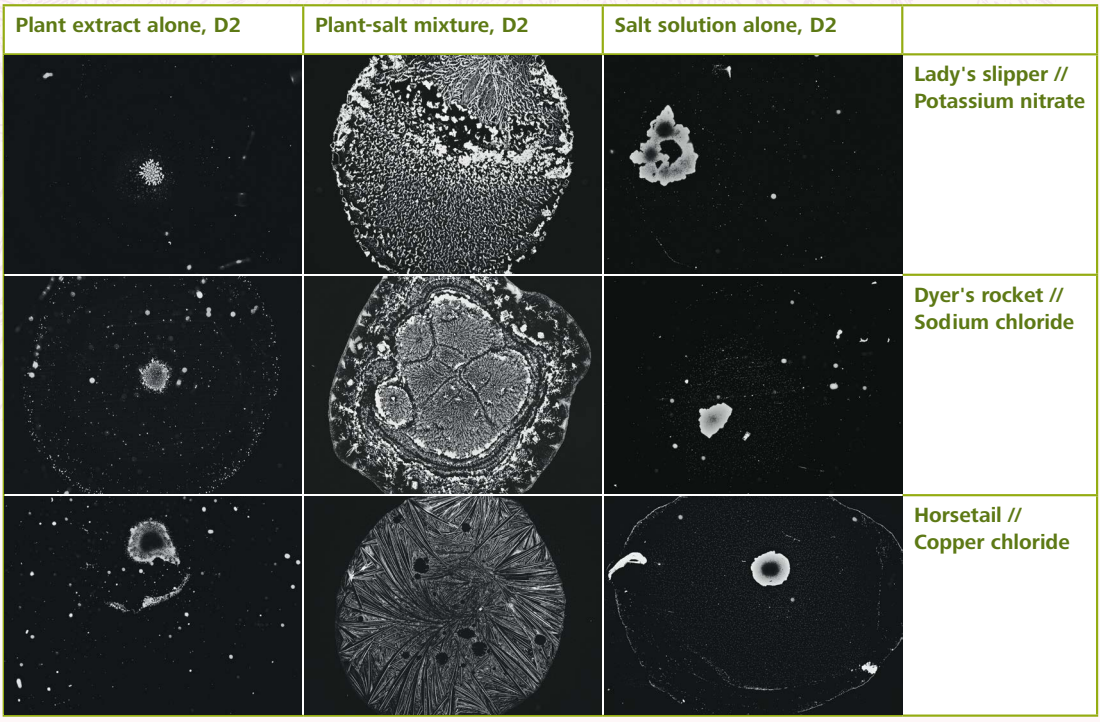

Fig. 1: The illustration shows the crystal patterns formed during evaporation, using examples of D2 potencies of individual plant extracts, salt solutions and their 1:1 mixtures. Each sub-image shows a droplet magnified 25 times (with a dark-field microscope).

D3 potencies (hundredfold and thousandfold dilutions) and to determine the influence of the plant and salt components on the crystal patterns of these mixtures that form during the drying of the drops.

Using the droplet evaporation method, we analysed seven plant extracts and five salt solutions (see Table 1) in D2 or D3 potencies and their 1:1 mixtures. Drops of each sample were placed on a glass slide and allowed to evaporate. The resulting crystal patterns were photographed using a dark-field microscope at 25× and 100× magnification. Examples of such photographs can be seen in Fig. 1.

As expected, the crystalline structures from the samples at the lower potency (D2) exhibited significantly richer and more numerous forms than those of the samples in D3. Interestingly, the mixtures of plant extracts and salt solutions at both potency levels produced entirely new forms that could not be derived from the sum of the forms of their individual components. In most cases, the forms of the mixtures were also much richer than those of the individual components. We were able to see the well-known quote from Aristotle, 'the whole is greater than the sum of its parts', confirmed here on a qualitative level.

This study demonstrates that the droplet evaporation method has the potential to characterise multi-component mixtures qualitatively and to describe the differences from their individual components. The study provides a solid starting point for further investigations into homeopathic complex remedies and other multi-component mixtures. ■

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Interview with the Head of Tumour Biology and Pharmacology Research Group

DR. PETRA KERN, DR. ULRIKE WEISSENSTEIN

Dr. Ulrike Weissenstein has been working at the Society for Cancer Research (SCR) for 20 years. Now she looks back on her research work and her achievements.

Dr Weissenstein, how did you come to join the SCR?

After completing my biology degree and PhD at Martin Luther University Halle-Wittenberg in Germany, my path first took me to Switzerland, where I gained valuable scientific experience as a postdoctoral researcher at Sandoz in Basel. As I was very interested in tumour research and the possibilities of integrative cancer treatment, I was delighted to subsequently take up my first position at the SCR. After maternity leave and a few professional stints at other research institutions, I returned to the SCR – this time with my own research project on circulating tumour cells. Shortly afterwards, I took over as head of the tumour biology and pharmacology research group.

What were the first questions you addressed?

In an early project, my research group looked at tumour cells circulating in the blood of cancer patients, and we established a method of making these cells visible under a microscope. Outside our study, however, this rather labour-intensive method was not used further.

Dr. Ulrike Weissenstein preparing samples in the cell culture laboratory.

Another focus lay on investigating the effect of the fat-soluble mistletoe extract VALE (*Viscum album* lipophilic extract) on human immune cells. As part of master's and doctorate theses, we analysed how VALE influences the migration of certain cell types found in the skin (fibroblasts and keratinocytes), and experiments were conducted to investigate wound healing

processes. A doctoral student investigated whether VALE has an effect on the function of certain immune cells, namely macrophages, which were cultured together with tumour cells. These projects demonstrated how the lipophilic mistletoe extract modulates immune and regenerative mechanisms and what the significance could be for future therapeutic approaches.

Supporting and mentoring young researchers during their bachelor's, master's and doctoral theses is particularly important to me. It is a joy to see young people tackling a research question with such enthusiasm, and we have consistently achieved excellent results that have advanced our research.

Have you also worked with the mistletoe preparation Iscador?

Yes, my group investigated the mistletoe preparation Iscador in preclinical tumour cell models. In a series of projects and publications, we systematically investigated interactions between standardised mistletoe extracts and conventional cancer therapies in order to identify both positive and negative interactions and to assess the safety of combined treatments. Our results showed that mistletoe preparations do not reduce the efficacy of the tested cancer drugs (chemotherapeutics, Herceptin and Tamoxifen), but in some cases exert complementary effects. Nor were we able to detect any inhibition by Iscador of relevant cytochrome P450 enzymes involved in the metabolism of drugs in the liver. Overall, the cell culture data suggest that mistletoe preparations can be safely combined with the cancer drugs studied and, in some cases, exhibit complementary effects. All of this reinforces the importance of mistletoe therapy as a complementary approach, particularly with regard to its safety when used concurrently with standard oncological treatments.

Does your group also collaborate with external groups?

Yes. Examples of successful collaborations with external partners include bachelor's, master's and doctoral theses carried out in collaboration with the Universities of Basel and Witten-Herdecke and the University of Applied Sciences Northwestern Switzerland.

Another example is our collaboration with researchers at the University of Rio de Janeiro in Brazil on projects involving a mistletoe-containing hydrogel for topical application and phytochemical analyses of alcoholic mistletoe extracts.

What was your latest research finding?

In recent years, new immunotherapies have been developed and approved, which led me to ask what role mistletoe therapy might play in the context of these modern forms of treatment. The specialist literature describes how certain therapies trigger what is known as *immunogenic cell death* (ICD) – a form of cell death that can activate a specific anti-tumour immune response in the body. At the same time, there is debate as to whether the combined intratumoural administration of such ICD-inducing substances could enhance the efficacy of systemic immunotherapies or reduce their dosage, which in turn would potentially mitigate severe side effects. As there

are numerous case reports of successful intratumoral mistletoe treatments, I wondered whether mistletoe preparations could also trigger immunogenic cell death. We tested this hypothesis in our laboratory on various cancer cell lines and recently successfully concluded the project with a scientific publication. Our study demonstrated for the first time that a fermented mistletoe extract can trigger typical signals of immunogenic cell death in cell culture – that is, a form of tumour cell death that activates the immune system. These include stress responses within the cell, the appearance of characteristic alarm molecules on the cell surface, as well as the release of signalling molecules such as ATP.

What question will you be tackling next?

Our findings represent an important first step, as they suggest that mistletoe extracts may, basically, be capable of stimulating an immune response against tumour cells. However, it remains to be seen whether this effect also occurs in the human body. In our next studies, we aim to clarify whether the dying cancer cells treated with mistletoe extracts actually activate immune cells, such as dendritic or T cells, and could thus stimulate the body's own cancer defence mechanisms. If this effect can be confirmed in laboratory trials, it would suggest that intratumoural mistletoe application could be a promising approach – particularly as a complement to existing immunotherapies.

Thank you very much for speaking with us, and we wish you every success with your future research, Dr Weissenstein! ■

Would you like further information on this topic? Please contact Ulrike Weissenstein: u.weissenstein@vfk.ch

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