Report 2022

Society for Cancer Research
Arlesheim • Switzerland

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.

Executive Board Members:
Professor Stephan Baumgartner
Dr Hartmut Ramm
Dr Gerhard Schaller

Society for Cancer Research
Verein für Krebsforschung
Kirschweg 9
CH-4144 Arlesheim
Switzerland

Web: www.vfk.ch
E-mail: info@vfk.ch
Phone: +41 (0) 61 706 29 29
Fax: +41 (0) 61 706 72 00

Contents

Editorial

Dear Readers

One of the main goals of the Society for Cancer Research is to develop therapies for people affected by cancer. The basis for these therapies is the intimate relationship between the human being and nature, their mutual interweaving as well as their mutual dependence. This relationship is being repeatedly exposed to threats, especially from many aspects of our contemporary lifestyles and the assumption that nature holds resources which are inexhaustible and may be exploited accordingly.

The staff of the Society for Cancer Research is taking a different approach here. The new project «Therapeutic Landscapes» may serve as an example. Annika Mascher and Hartmut Ramm report on a pilot project whose aim it is to create a new relationship between humans and nature in cooperation with people affected by cancer. A decisive moment in this process is to not simply 'consume' nature, but to encounter it in a mindful way and thereby gain inspiration for inner processes of consciousness and development. Thus, the aim of this encounter is not only the healing of human beings, but also of their relationship with nature, and therefore also a contribution to the healing of nature itself.

There are many impulses from anthroposophic pharmacy for the development of new medicines for integrative oncology. In the contribution by Daniel Krüerke and Karolina Königsberger, an evaluation of the clinical application of a mistletoe resin cream is presented. This cream - a new medicine developed by the Society for Cancer Research – has been used for the treatment of actinic keratoses, basal cell carcinomas and squamous cell carcinomas and has shown promising results. Three further articles (by Bettina Leonhard, João Batista and Ulrike Weissenstein) report on various aspects of a drug development project aimed at using the therapeutic potential of larch resin. There is a long way to go from the raw material to the final product. Three stations on this path are reported: the trees in East Tyrol, laboratory tests and the necessary chemical analysis.

Anthroposophic medicine is based on a complex, multi-layered fabric of different

therapies. Evaluations, especially of anthroposophic oncology, must therefore include the whole range of all these therapies; studies on individual therapies alone could underestimate their potential if additive or synergistic effects are present. Daniel Krüerke shows in his article that patients treated for longer periods in anthroposophical clinics showed above-average survival times. One of the essential goals of the Society for Cancer Research is to document this phenomenon more precisely in the future and to develop the potential of anthroposophic medicine in oncology even further.

Professor Stephan Baumgartner

Executive board member of the
Society for Cancer Research

Professor Stephan Baumgartner
Head of Research and Development
E-mail: st.baumgartner@vfk.ch

Society for Cancer Research
Hiscia Research Institute
Kirschweg 9
CH-4144 Arlesheim

First Experiences in the Pioneering Project «Therapeutic Landscapes»

ANNIKA MASCHER, HARTMUT RAMM

In a guided group work, cancer patients were invited to connect in a new way with their remedy, mistletoe. The mindful immersion into the outer landscape has helped them explore new aspects of their soul's inner landscape. Nature can thus become a «green coach».

The idea of visiting natural landscapes for therapeutic purposes is not new, but only arrived in the academic world 30 years ago, where a broad field of research has since been established [1-3]. In Referencese, however, only a few studies with cancer patients address experiences with landscape-based therapies – from psycho-neuro-immunological effects to spiritual experiences [4-8]. In contrast to forest bathing or similar therapies, our new project «Therapeutic Landscapes» is not only about the pure effect of nature on the participants but is above all about giving people stimuli for inner processes through a landscape shaped by mistletoe. What we set in motion by practising together as a group then leads to independent deepening. So far, the conventional medical system has hardly been able to cover such aspects. But they are urgently needed to support people as whole beings on the path of their recovery.

In 2022, we were able to gather initial experiences with a small group within the framework of this project. Six times over the course of the year we met with five cancer patients outside, in nature. The first and last meeting took place in the mistletoe garden of the Hiscia Research Institute. In between, the joint practice unfolded at «Disli», our oldest location, where the Society for Cancer Research has been cultivating mistletoe since 1976. The meetings showed that this site offers optimal conditions for patients to enter into a focused perception and mindfulness of the present moment, into inner processes as well as a dialogue with themselves, nature, the earth, mistletoe and the group. As one participant reflected: *«The illness is not in the*

On the way to the mistletoe cultivation site – protected in an idyllic valley

Sculpting with clay which occurs naturally at the site

focus, we have really come into relationship with you, the Disli and the mistletoe.» Another participant summed up: *«I have become a different person since spring. I have a different understanding of mistletoe and Iscador.»*

Perception exercises (with different senses, nature contemplation, group exercises), meditations (in stillness and movement) and sculpting with clay that naturally occurs at Disli, proved to complement each other. Between the liveliness and calm of the exceptional nature at this cultivated site, something deeply moving emerged in the guided group work that led into stillness and addressed fundamental aspects of healing and self-development. This was evident in impressions such as *«being allowed to feel oneself again, being away from the noise»*, or *«coming into being through the feet»* during a walking meditation. One participant described: *«An impressive silence and simultaneous alertness arose immediately. Having the mistletoe so close to me, hanging between heaven and earth and well anchored in the uprightness of the tree, radiated a sense of security. Walking barefoot on the ground also allowed me to connect with the growing and withered nature. It also just gave me a strong sensation of being alive.»*

The participants developed new perspectives on themselves and a new way of experiencing themselves in the environment - their inner landscape became similarly

Mindful observation on a walking meditation – the outer nature and the inner condition

tangible, as did the outer landscape. The joint practice and research was carried by the whole group, which grew closer together in the course of the meetings, deepening the process even more.

What happens when people create a relationship between themselves and their remedy instead of just *«consuming health»*, as one participant described? These are questions we will continue to explore together. The pioneer group not only experienced the joint research with *«enormous gratitude»,* but also formulated it as an aspiration to become deeper involved with mistletoe. In other words, *«not just to take a medicine, but to accompany it with awareness»*. Accordingly, after the winter mistletoe, our pioneer group will also harvest the summer mistletoe from elm trees and experience the production of Iscador.

In the future, we would like to further deepen our support of cancer patients in experiencing their inner as well as outer landscape in order to strengthen their self-regulation and resilience, also in cooperation with Klinik Arlesheim. ■

Dr. med. univ. Annika Mascher
Society for Cancer Research
Hiscia Research Institute
Clinical Research Department
E-mail: a.mascher@vfk.ch

Dr Hartmut Ramm
Society for Cancer Research
Hiscia Research Institute
Botanical Department
E-mail: h.ramm@vfk.ch

References

1. Bell SL, Foley R, Houghton F, Maddrell A, Williams AM (2018) From therapeutic landscapes to healthy spaces, places and practices: A scoping review. Social Science and Medicine 196, 123-130. DOI: 10.1016/j.socscimed.2017.11.035.
2. Gebhard U, Kistemann T (2016) Landschaft, Identität und Gesundheit: Zum Konzept der Therapeutischen Landschaften. Wiesbaden: Springer.
3. Park S, Kim E, Kim G, Kim S, Choi Y, Paek D (2022) What activities in forests are beneficial for human health? A systematic review. International Journal of Environmental Research and Public Health 19(5):2692. DOI: 10.3390/ijerph19052692.
4. Blaschke S (2017) The role of nature in cancer patients' lives: a systematic review and qualitative meta-synthesis. BMC Cancer 17(1):370. DOI: 10.1186/s12885-017-3366-6.
5. Cimprich B, Ronis DL (2003) An environmental intervention to restore attention in women with newly diagnosed breast cancer. Cancer nursing 26(4), 284-292. DOI: 10.1097/00002820-200308000-00005.
6. English J, Wilson K, Keller-Olaman S (2008) Health, healing and recovery: therapeutic landscapes and the everyday lives of breast cancer survivors. Social Science and Medicine 67(1), 68-78. DOI: 10.1016/j.socscimed.2008.03.043.
7. Li Q, Morimoto K, Kobayashi M, et al. (2008) Visiting a forest, but not a city, increases human natural killer activity and expression of anti-cancer proteins. International Journal of Immunopathology and Pharmacology 21(1), 117-127.
8. Pascal J (2010) Space, Place, and Psychosocial Well-Being: Women's Experience of Breast Cancer at an Environmental Retreat. Illness, Crisis & Loss 18(3), 201-216. DOI: 10.2190/IL.18.3.c.

Harvesting Larch Resin in East Tyrol

BETTINA LEONHARD

Experiencing the larches in their natural environment and gaining insight into the tradition of resin harvesting made it possible to create a connection with the pharmaceutical raw material, larch resin, and its mindful extraction and processing.

One of the central tasks of the Hiscia Research Institute at the Society for Cancer Research is the pharmaceutical development of new medicinal products for the treatment of cancer patients. Thus, based on suggestions by Rudolf Steiner on the treatment of exulcerating tumour wounds, a new pharmaceutical formulation was created in our project: a cream made of larch resin (larch turpentine from *Larix decidua* Mill.), moneywort (*Lysimachia nummularia* L.), thyme (*Thymus vulgaris* L.) and beeswax. As described in the subsequent article by João Batista, larch resin is the focus of his research project. A considerable part of this project involves the specific selection of the larch resin to be used. For this purpose, resins from different origins and suppliers are analysed to obtain information about their composition as well as their antimicrobial and wound healing properties.

Fig. 1 above: *Lienz Dolomites*
Fig. 2 right: *Larch grove in the Villgratental valley*

Fig. 3: *Larch with borehole*

Fig. 4: *Batista with resin spoon*

Fig. 5: *Freshly extracted resin*

We travelled to East Tyrol in Austria to experience the harvesting of larch resin in its natural environment and to investigate the significance of this raw material's origin. The larch resin is extracted from the region's vast natural larch population. Thanks to a traditional distillery, we were able to gain valuable insights into the art of larch resin harvesting. The excursion to the larches in the picturesque Villgratental (Fig.2) at 1400 m above sea level was not only a soothing nature experience, it also showed us the importance of treating the trees with care so that they may serve us sustainably as a source of «liquid gold».

When the trunk has reached a circumference of 40-50 cm, a hole is drilled into the tree (Fig. 3) and closed with a wooden cone made of larch wood. The resin is extracted only 1-2 years later during the months of May and September. For this purpose, the closed borehole is opened and via the rotation of a metal «resin spoon» (Fig. 4) the resin is harvested from the tree.

The collected resin (Fig. 5) is heated in larger quantities in the local factory and impurities are removed by filtration. About 200 to 300 g of resin can be collected from a tree each year over an average period of 10-15 years. For quality control and for certification, a part of the resin is subjected to steam distillation in order to characterise its essential oils by means of gas chromatography.

We thank the generous and warm-hearted employees of the distillery for giving us this insight into their ecologically run business and for sharing with us the beauty of nature, which is last but not least the basis for the resin in the cream we have developed.

This excursion to the larches in their natural environment as sources of the precious resin substance, which oozes out of the trunks like honey, has helped us approach the identity of this tree and its substances. With this experience in mind, we will be able to introduce the larch resin with greater respect into the pharmaceutical process together with the other components in order to form a new healing unity. ■

Bettina Leonhard
Society for Cancer Research
Hiscia Research Institute
Pharmaceutical Development Department
E-mail: b.leonhard@vfk.ch

Larch Resin as an Active Ingredient for the Future Treatment of Chronic Wounds

JOÃO BATISTA

The resin extracted from European larch is at the centre of an ongoing PhD thesis. Several larch resin batches have been chemically analysed for non-volatile diterpenes and volatile monoterpenes. The aim is to use larch resin to develop a new pharmaceutical formulation for the treatment of chronic wounds.

The development and improvement of pharmaceutical formulations is necessary and of great importance for the treatment and well-being of cancer patients. As mentioned in the previous article [1], we have started the development of a new formulation with four natural components for the treatment of exulcerating tumour wounds. These chronic wounds are associated with impaired quality of life at physical, social and psychological levels in advanced stage cancer patients [2]. The current pharmaceutical formulation, a cream (Resina laricis, Lysimachia comp. Crème), is available as a compounded medication on prescription at the pharmacy of Klinik Arlesheim. Although the first experiences with this cream are promising, a new pharmaceutical formulation is necessary because complex wounds are difficult to treat and a cream cannot always be easily applied to the entire wound surface. I am therefore writing my PhD thesis on a formulation, which is easier to apply (e.g. a spray), thus serving the patients and offering healthcare professionals a wider range of choices for the treatment of exulcerating tumour wounds as well as other chronic wounds, such as pressure ulcers and diabetic ulcers.

An important ingredient suggested by Rudolf Steiner for this formulation is larch resin [3], a yellowish translucent, sticky resin derived from an alpine conifer, the European larch (*Larix decidua* Mill.), which belongs to the Pinaceae family (Fig. 1). In our recent review article [4], we found two publications on the ethnobotanical use of the resin for various conditions, including wound healing and ulcers. In addition, topical application, e.g. in the form of a cream containing 10-20% larch resin, has already been approved for treating wounds in veterinary medicine [5]. Although this clinical use was already suggested by Paracelsus [6], we could not find any scientific data on it. This is all the more surprising as the larch resin contains several interesting chemical compounds, especially diterpenes and monoterpenes, which have anti-inflammatory and antimicrobial properties. Taking into account the popular use of the resin and the available scientific information, we are currently studying differ-

Fig. 1: *Larches in their natural habitat A. Larches in autumn B. The needles turn from green to yellow in autumn C. Young tufts of needles at the beginning of summer D. Needles and young cone in summer*

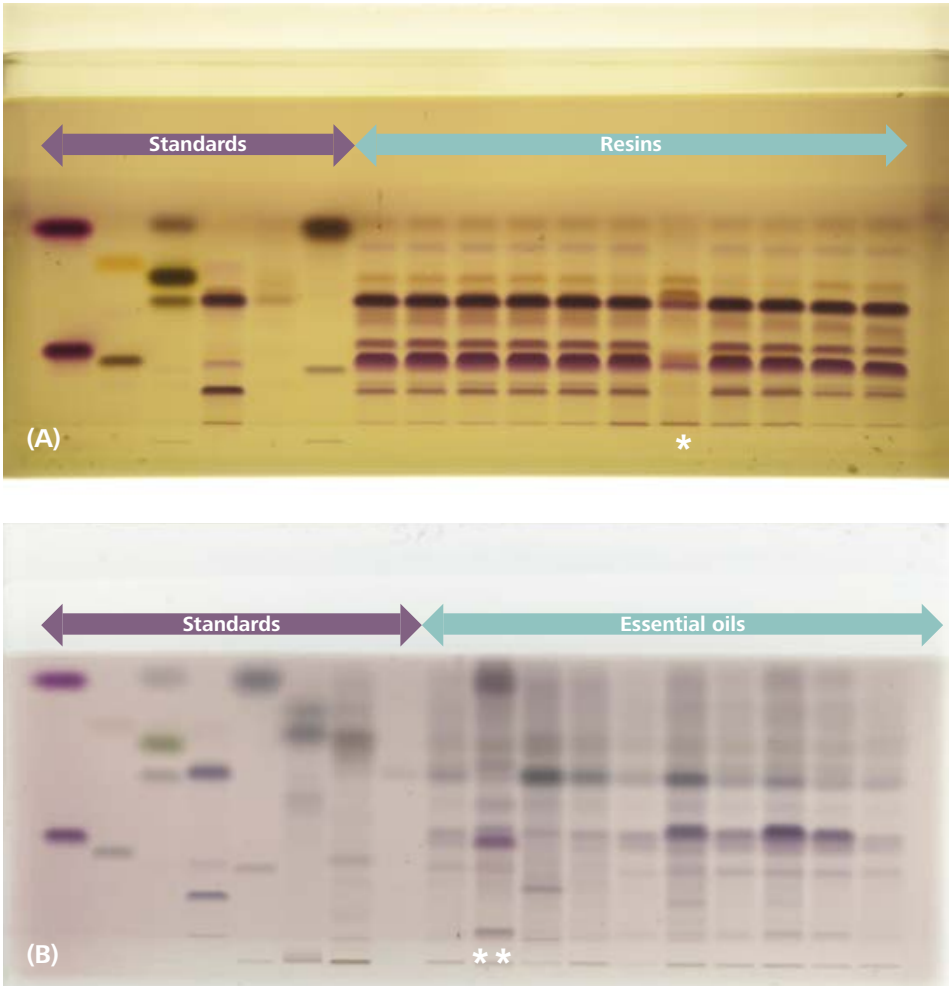


Fig. 2: *HPTLC plates of the resins (A) and the essential oils (B)*
** mixed adulterated resin ** essential oil from the needles*

ent batches and origins of larch resin: their chemical variability and their cytotoxic and antimicrobial activities. This will allow us to investigate the relationship between the properties of the resin and its wound-healing effect. In parallel, we are developing a nanoemulsion to obtain a spray to cover large wound surfaces.

One way to analyse the chemical composition of a larch resin is to extract its essential oils by distillation. While the HPTLC method yielded an almost identical profile for resins of different origins, the essential oils of the same resins showed great differences (Fig. 2). These results indicate a typical pattern of non-volatile components (diterpenes) and a variation of volatile components (monoterpenes), which may cause differences in biological activity. Another interesting result is that the viscosity of each resin correlated with their essential oil content.

These results lay the foundation for the further development of the larch resin spray in an academic context. They are also essential to improve our understanding of this complex substance's mode of action. We therefore also include the therapeutic concepts of anthroposophic medicine. ■

References

1. Leonhard B: Larch harvesting in East Tyrol, in this issue, p. 10 ff.
2. Falanga V, Isseroff RR, Soulika AM, Romanelli M, Margolis D, Kapp S, Granick M, Harding K (2022) Chronic wounds. Nature Reviews Disease Primers 8(1):50. DOI: 10.1038/s41572-022-00377-3.
3. Krüger H (1969) Resina laricis / Larix decidua. In: Medizinische Sektion der Freien Hochschule für Geisteswissenschaft am Goetheanum (Hrsg.) Heilmittelangaben Rudolf Steiners. Dornach
4. Batista JVC, Uecker A, Holandino C, Boylan F, Maier J, Huwyler J, Baumgartner S (2022) A scoping review on the therapeutic potential of resin from the species Larix decidua Mill. [Pinaceae] to treat ulcerating wounds. Frontiers in Pharmacology 13:895838. DOI: 10.3389/fphar.2022.895838.
5. Committee for Veterinary Medicinal Products (1998) Terebinthinae laricina, summary report. The European Agency for the Evaluation of Medicinal Products, EMEA/MRL/398/98: London: European Medicines Agency.
6. Rippe O, Madejsky M (2006, eds.) Die Kräuterkunde des Paracelsus. AT-Verlag, Munich.

João V. C. Batista, M.Sc.
Society for Cancer Research
Hiscia Research Institute
Pharmaceutical Development Department
E-mail: j.dacostabatista@vfk.ch

When Patient Data Improves Medical Knowledge

DANIEL KRÜERKE

Since 1949, thanks to their consent, patients' courses of disease have been documented at Lukas Klinik and Ita Wegman Klinik (i.e. today's Klinik Arlesheim). Over time, these files resulted in an extensive data archive, which can now be analysed using modern statistical methods.

In order to learn more about cancer and treatment effects, information on new cases, disease severity, treatments and survival times is collected in special cancer registries. The first local cancer registries were developed as early as the 19th century. Today, large comprehensive national and international patient data collections exist. These data can help to validate therapies and to identify particular patient characteristics which may be associated with longer survival times.

In order to assess and validate mistletoe therapies, Lukas Klinik and Ita Wegman Klinik started documenting the courses of disease observed in their oncological departments. In response to the clinic doctors' explicit request, a cancer registry was established as early as 1949. The data released by patients signing a declaration of consent for further use in research and thus made available to doctors and scientists, became more and more extensive. Initially, the registries consisted of simple index card systems which later were automated (Fig. 1).

From the 1990s onwards, computers came into use. A scientist from the Society for Cancer Research programmed the so-called «aftercare database» for the Lukas Klinik, which was maintained until 2017. This database contains selected data from the disease courses of over 38,000 patients, the first of which was documented at the beginning of the 1950s. Between 2008 and 2019, more than 8,000 patients' cases were also documented in the oncology database «QuaDoSta» (Quality, Documentation and Statistics), sometimes very extensively. This special database was developed at the Havelhöhe Research Institute in Berlin and operated in long-standing cooperation with the Society for Cancer Research [1]. Everything changed, however, when Lukas Klinik and Ita Wegman Klinik merged to form Klinik Arlesheim, the im-

Fig. 1: *Structure of the old paternoster hanging register at Lukas Klinik, which was operated until about 1990, with organ areas as well as information on recurrences and therapy forms*

plementation of the new Swiss Human Research Act (2014) and the introduction of electronic medical records in hospitals (2016). Since then, a new declaration of consent (a so-called «general consent») signed by the patient makes all the digital clinical data available for research, and the cumbersome, error-prone transfer from paper files to another system is no longer necessary.

As a result, two databases exist today: one extensive database from the historical archives and one database rapidly growing from the clinic's current digital information system. These sources provide data of varying scope and quality, which can help answer scientific questions related to real treatments that have taken place.

Last year, we published a feasibility study of survival analyses using these data[2]. For this purpose, we used data on diagnosis, admission and survival times of patients with breast cancer and pancreatic cancer. It turned out that as a whole, the survival times of these patients are comparable with those of the large cancer registry of the Robert Koch Institute. However, if one takes into account the duration of patients' treatment at Lukas Klinik or Ita Wegman Klinik, survival times increased the longer this period was in relation to the time passed since diagnosis. This suggests that something is happening in the clinics that may prolong the lives of the patients. In a next step, we would like to investigate this exciting finding with advanced data analysis. Results from such work could provide us with valuable clues to target specific efficacy studies and to further improve our medications and therapies.

Finally, for as long as these data sources have existed, they have offered us numerous and useful insights. They have been used in research, have led to several publications and (despite all criticism regarding digitalisation) will be of even greater benefit to us in the future, thanks to this positive use of digitalisation. ■

References

1. Jeschke E, Schad F, Pissarek J, Matthes B, Albrecht U, Matthes H (2007). QuaDoSta - ein frei konfigurierbares System zur Unterstützung multizentrischer Datenerhebungen in medizinischer Versorgung und Forschung. GMS Medizinische Informatik, Biometrie und Epidemiologie 3(2):Doc10.
2. Ostermann T, Appelbaum S, Baumgartner S, Rist L, Krüerke D (2022). Using merged cancer registry data for survival analysis in patients treated with integrative oncology: Conceptual framework and first results of a feasibility study. In: Proceedings of the 15th International Joint Conference on Biomedical Engineering Systems and Technologies 5 – HEALTHINF, 463-468. DOI: 10.5220/0010826400003123.

Dr Daniel Krüerke
Society for Cancer Research
Hiscia Research Institute
Clinical Research Department
E-mail: d.krueerke@vfk.ch

Application of a Cream with Mistletoe Resin

A Retrospective Case Series on Treatments of Actinic Keratosis, Squamous-cell Carcinoma of the Skin and Basal Cell Carcinoma

DANIEL KRÜERKE, KAROLINA KÖNIGSBERGER

In the context of a doctoral thesis, the effect of a cream with mistletoe resin in the topical treatment of actinic keratosis, squamous-cell carcinoma and basal cell carcinoma was investigated. Retrospective case analyses provide first evidence that the cream effected partial or complete remission in up to 71% of the skin lesions treated. Further research is necessary to confirm this result.

Actinic keratoses are skin alterations caused by UV-light, which can develop into squamous cell carcinoma. Squamous cell carcinoma of the skin is the second most common malignant, non-melatonic skin cancer after basal cell carcinoma. Both belong to the group of the so-called «white» or «non-pigmented» skin tumours, and their standard therapy is surgical removal. However, there are some patients for whom surgery is not possible, e.g. due to concomitant diseases, advanced age or personal preference. Also, surgery may not always be recommended in case of large or unclear lesions or lesions occurring in sensitive areas. In such cases, radiation or drug therapies are considered.

So far, mainly superficial basal cell carcinomas and in rare cases non-infiltrating squamous cell carcinomas have been treated externally. Other types of non-pigmented skin tumours have rarely been treated externally. Thus, there is a need for effective and tolerable external treatment options for the wide range of such tumours.

In the 2018 annual report, a newly developed cream with mistletoe resin was presented which requires the fat-soluble ingredients of the white-berry mistletoe (*Viscum album* L.) for its production. The extraction method used is a modern extraction process using supercritical carbon dioxide, enabling the fat-soluble total ex-

(a)

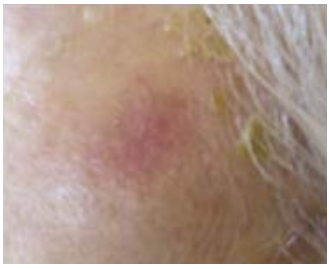
23.08.2017

03.01.2018

(b)

17.01.2020

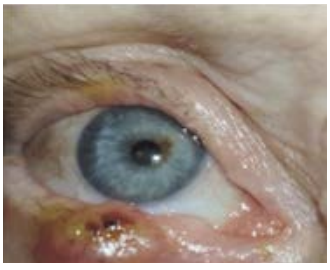
01.04.2020



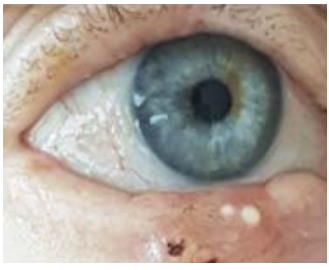
13.07.2020

(c)

26.09.2018



09.05.2019



04.07.2019

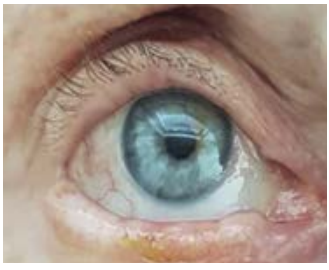


Fig. 1: *Exemplary course of disease of actinic keratosis (a), squamous cell carcinoma (b) and basal cell carcinoma (c) under the application of the new mistletoe resin cream*

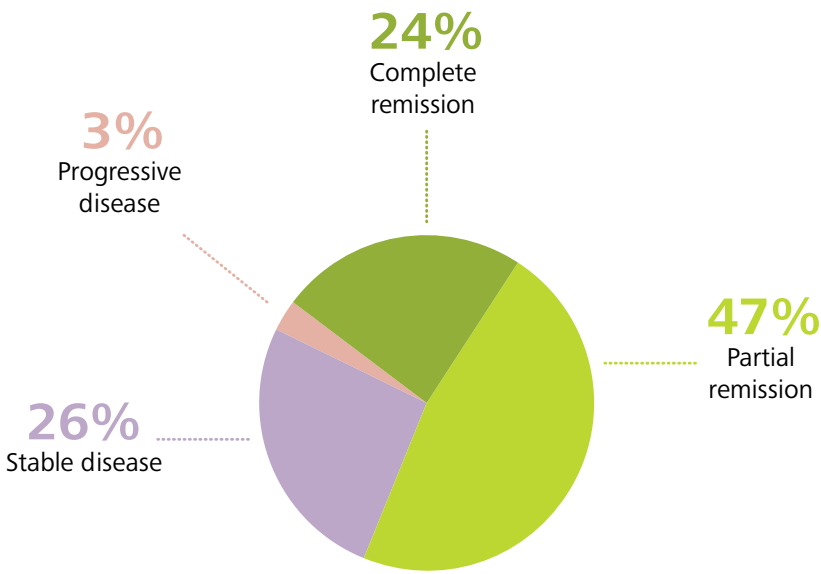


Fig. 2: *Therapeutic effect of mistletoe resin cream in the treatment of all 74 skin lesions (48 actinic keratoses, 9 squamous cell and 17 basal cell carcinomas)*

tract of mistletoe to be obtained gently, in high yield and completely solvent-free. Medical observations of applying this cream in the treatment of the above-mentioned skin tumours showed good results.

Now, a retrospective case series study was conducted for this cream. For this purpose the disease courses of 55 patients with 74 skin lesions caused by actinic keratosis, squamous cell and basal cell carcinomas, which were treated with the mistletoe resin cream, were examined (Fig. 1).

The clinical response analysis of the 74 treated skin lesions showed complete remission in 24%, partial remission in 47%, growth arrest in 26% and disease progression in 3% (Fig. 2). These results have to be confirmed via further research. With a treatment duration of 25-55 weeks, a medium probability of the best clinical response was achieved.

The following adverse effects were reported in five patients: skin redness and inflammatory reactions of mostly moderate severity, which resolved completely. In one case, the therapy was temporarily paused, in four cases it was continued without interruption.

The results of this study indicate that the use of this mistletoe resin cream is safe and well-tolerated when applied under medical supervision. First results indicate also that the application of this cream can lead to a therapeutically favourable course of disease. A manuscript with the results was submitted for publication in an international scientific journal. In her doctoral thesis, Karolina Königsberger, who has now successfully completed her doctorate, recommends as further step a controlled clinical study in which the efficacy and non-inferiority of this mistletoe resin cream compared to other drugs for external treatment could be proven. ■

References

Königsberger KM (2022) Anwendung eines Harz-Extraktes aus Viscum album bei aktinischer Keratose, kutanem Plattenepithelkarzinom und Basalzellkarzinom – eine multinationale, retrospektive Fallserienstudie. Dissertation zur Erlangung des Doktorgrades der Medizin, Universität Witten/Herdecke.

Urech K, Schaller G, Maier J (2018) Two new preparations for use in oncology practice – from the Pharmaceutical Development department of Hiscia Research Institute. Report Society for Cancer Research 38-43.

Urech K, Maier J (2021) Mistelharz: Zukunftspotenzial der onkologischen Misteltherapie. Der Merkurstab 74(6), 499-505. DOI: 10.14271/DMS-21429-DE.

Dr Daniel Krüerke
Society for Cancer Research
Hiscia Research Institute
Clinical Research Department
E-mail: d.krueerke@vfk.ch

Dr Karolina Königsberger
Klinik Arlesheim, Internal Medicine Department
E-mail: karolina.koenigsberger@klinik-arlesheim.ch
www.klinik-arlesheim.ch

Validation of a Pharmaceutical Analytical Method and Cell Culture Experiments for the Further Development of Wound Healing Preparations

ULRIKE WEISSENSTEIN, JOÃO BATISTA

In his master's thesis, a pharmacy student developed an analytical method for specific volatile compounds in larch resin. In addition, he examined the safety of larch resin and thyme extracts on skin cells in vitro.

Rudolf Steiner proposed a topical medication made from larch resin (larch turpentine from *Larix decidua* Mill.), moneywort (*Lysimachia nummularia* L.), thyme (*Thymus vulgaris* L.) and beeswax for the treatment of exulcerating tumour wounds[1]. In his master thesis, the pharmacy student Alain Bugnon contributed to the research on this formula by conducting analytical tests and cell culture investigations with the lipophilic components of larch resin and thyme CO_2 extract.

His work joins a series of previous master's theses on this subject: literature searches have been compiled, an experimental cream has been developed and made available to physicians as a compounded medication. As a first assessment of its efficacy, antitumor effects of moneywort and thyme extracts have been previously investigated in cell culture experiments (for a research summary, see the Annual Report of the Society for Cancer Research 2021).

For launching a new topical medication, like any other medical preparation, federal authorities require validated analytical methods for quality control. These analytical procedures can also be used to accurately and reliably select the optimal larch resin for the new formulation. Alain Bugnon developed and tried to validate a gas chromatographic (GC) method to quantify two volatile compounds, alpha-pinene and 3-carene, in an essential oil obtained by steam destillation of a European larch resin. The developed GC method is selective, linear and sensitive for both compounds. The precision and accuracy are in acceptable ranges. The recovery rate, however, is out of the acceptable limits for both compounds and therefore requires further research.

Fig. right: *European larch (Larix decidua Mill.)*

The mentioned GC method still has to be optimized for the use of an internal standard instead of an external standard as it currently does. In addition, further experiments are currently performed to improve our understanding of the composition of the different essential oils obtained from larch resin.

The aim of Alain Bugnon's cell culture experiments was to find out whether the lipophilic thyme and larch extracts caused cell death or reduced cell division. The skin cell types used for this experiment, fibroblasts (mouse cell line NIH/3T3) and keratinocytes (human cell line HaCaT) play an important role in wound healing. It is therefore important to demonstrate that the new topical formula does not damage these cells. Fibroblasts, the predominant cell type in connective tissue, are involved in all phases of wound healing. In wound tissue, they produce the 'scaffold' of the skin, the extracellular matrix and the collagen structures. Fibroblasts also support other cell types during wound healing [2]. Keratinocytes are the protective cells on the wound surface: they migrate during the skin remodelling phase from the lower levels of the skin to the surface in order to cover it.

The experiment results showed that both extracts caused cell death and reduced cell division in a concentration-dependent manner. These results will be taken into account in the development of further pharmaceutical formulations for the treatment of exulcerating wounds. Future clinical studies must confirm that the components of this topical formula do not cause skin irritation or damage.

Future investigations will collect further evidence on the four components' suitability for the use proposed by Rudolf Steiner. These will include wound healing experiments and the investigation of anti-microbial properties. ■

References

1. Krüger H (1969) Resina laricis / Larix decidua. In: Medizinische Sektion der Freien Hochschule für Geisteswissenschaft am Goetheanum (Hrsg.) Heilmittelangaben Rudolf Steiners. Dornach.
2. Bainbridge P (2013) Wound healing and the role of fibroblasts. Journal of Wound Care 22(8), 407-408, 410-412. DOI: 10.12968/jowc.2013.22.8.407.

Dr Ulrike Weissenstein
Society for Cancer Research
Hiscia Research Institute
Tumour Biology Department
E-mail: u.weissenstein@vfk.ch

João V. C. Batista, M.Sc.
Society for Cancer Research
Hiscia Research Institute
Pharmaceutical Development Department
E-mail: j.dacostabatista@vfk.ch

Publications of the Society for Cancer Research 2022

Acuña C, Mier y Terán A, Kokornaczyk MO, Baumgartner S, Castelán M	(2022) Deep learning applied to analyze patterns from evaporated droplets of Viscum album extracts. Scientific Reports 12(1):15332. DOI: 10.1038/s41598-022-19217-1.
Batista JVC, Uecker A, Holandino C, Boylan F, Maier J, Huwyler J, Baumgartner S	(2022) A scoping review on the therapeutic potential of resin from the species Larix decidua Mill. [Pinaceae] to treat ulcerating wounds. Frontiers in Pharmacology 13:895838. DOI: 10.3389/fphar.2022.895838.
Batista JVC, Bugnon A, de Moura P, Carvalho A, Leal I, Garrett R, Maier J, Boylan F, Holandino C, Huwyler J, Baumgartner S	(2022) Antimicrobial and phytochemical analyses of European Larch resins and essential oils. Planta Medica 88(15):1485. DOI: 10.1055/s-0042-1759122.
Bugnon A	(2022) Antiproliferative and apoptotic activity of larch resin and thyme extract. Development and validation of a GC-FID method to analyse larch essential oil. Master thesis, Philosophisch-Naturwissenschaftliche Fakultät Universität Basel.
De Oliveira Melo MN, Clavelland Ochioni A, Zancan P, Passos Oliveira A, Garrett R, Baumgartner S, Holandino C	(2022) Viscum album ethanolic extract promotes MDA-MB-231 cell death by glycolytic enzymes inhibition. Planta Medica 88(15): 1496-1497. DOI: 10.1055/s-0042-1759148.
Fritz J, Athmann M, Bornhütter R, Busscher N, Geier U, Mergardt G, Scherr C, Doesburg P	(2022) Analytical perception and kinesthetic engagement in evaluation of copper chloride crystallization patterns of wheat, grape juice and rocket samples from conventional, organic and biodynamic cultivation. Chemical and Biological Technologies in Agriculture 9:103. DOI: 10.1186/s40538-022-00361-9.

Gaertner K, Baumgartner S, Walach H	(2022) Is homeopathic Arnica effective for postoperative recovery? A meta-analysis of placebo-controlled and active comparator trials. Frontiers in Surgery 8:680930. DOI: 10.3389/fsurg.2021.680930.
Gannon C, Jäggy C	(2022) Goldener König und schwarzer Wolf. Alchemistische Bildsprache und Laborpraxis. Anzeiger EAS 26, 4-15.
Holandino C, Souza Rocha M, da Costa Batista JV, Emerich Bucco de Campos V, Passos Oliveira A, Baumgartner S	(2022) Viscum album hydrogel: physico-chemical evaluation and antiproliferative assay. Planta Medica 88(15): 1497. DOI: 10.1055/s-0042-1759149.
Königsberger KM	(2022) Anwendung eines Harz-Extraktes aus Viscum album bei aktinischer Keratose, kutanem Plattenepithelkarzinom und Basalzellkarzinom – eine multinationale, retrospektive Fallserienstudie. Dissertation zur Erlangung des Doktorgrades der Medizin, Universität Witten/Herdecke.
Melo MNO, Ochioni AC, Zancan P, Oliveira AP, Grazi M, Garrett R, Holandino C, Baumgartner S	(2022) Viscum album mother tinctures: Harvest conditions and host trees influence the plant metabolome and the glycolytic pathway of breast cancer cells. Frontiers in Pharmacology 13:1027931. DOI: 10.3389/fphar.2022.1027931.
Ostermann T, Appelbaum S, Baumgartner S, Rist L, Krüerke D	(2022) Using merged cancer registry data for survival analysis in patients treated with integrative oncology: Conceptual framework and first results of a feasibility study. In: Proceedings of the 15th International Joint Conference on Biomedical Engineering Systems and Technologies 5 – HEALTHINF, 463-468. DOI: 10.5220/0010826400003123.
Pelzer F, Loef M, Martin DD, Baumgartner S	(2022) Cancer-related fatigue in patients treated with mistletoe extracts: a systematic review and meta-analysis. Supportive Care in Cancer 30(8): 6405-6418. DOI: 10.1007/s00520-022-06921-x.

Rocha MS, Batista JVC, Melo MNO, Campos VEB de, Toledo ALMM, Oliveira AP, Picciani PHS, Baumgartner S, Holandino C	(2022) Pluronic F127 thermoresponsive Viscum album hydrogel: Physicochemical features and cellular in vitro evaluation. Pharmaceutics 14(12):2775. DOI: 10.3390/pharmaceutics14122775.
Ücker A, Baumgartner S, Martin D, Jäger T	(2022) Critical evaluation of specific efficacy of preparations produced according to European Pharmacopeia Monograph 2371. Biomedicines 10(3):552. DOI: 10.3390/biomedicines10030552.
Yousefvand S, Fattahi F, Hosseini SM, Urech K, Schaller G:	Viscotoxin and lectin content in foliage and fruit of Viscum album L. on the main host trees of Hyrcanian forests. Scientific Reports 12(1):10383. DOI: 10.1038/s41598-022-14504-3.
Zurbriggen L, Baumgartner S, Schaub N, Kokornaczyk MO	(2022) Influence of temperature and relative humidity on patterns formed in dried plasma and serum droplets. Colloid and Interface Science Communications 49:100645. DOI: 10.1016/j.colcom.2022.100645.

Impressum

Society for Cancer Research
Kirschweg 9
CH-4144 Arlesheim
Schweiz

Tel. +41 (0) 61 706 29 29
Fax. +41 (0) 61 706 72 00

Editor:
Florian Pelzer

Proofreading:
Corina Caminada

Design and Layout
Franziska Mbarga

Printing:
bc medien ag, Münchenstein

Picture Credits:
Hartmut Ramm: 5
Jürg Buess: 6, 21
Christoph Jäggy: 7, 8
Bettina Leonhard: 10, 11, 12
João Batista: 15, 16, 27
Daniel Krüerke: 19
Dorothea Schläpfer: 23

Changes of Address and Information:
Society for Cancer Research
Kirschweg 9
CH-4144 Arlesheim
Schweiz

E-mail: info@vfk.ch

Donations and Contributions

The Society for Cancer Research regards its activities as serving the public interest. We use your donations and contributions conscientiously to achieve our aim of developing holistic, effective and well-tolerated forms of natural cancer treatment. We thank you for your interest and your kind support. The Society for Cancer Research has charitable status in Baselland Canton, Switzerland. Donations to the Society for Cancer Research are by law tax-deductible in Switzerland. A receipt will be issued for all donations.

Bank Account
Society for Cancer Research
Verein für Krebsforschung
Kirschweg 9
CH-4144 Arlesheim

Basellandschaftliche Kantonalbank
IBAN: CH07 0076 9050 7004 3200 1
BIC/SWIFT: BLKBCH22

www.vfk.ch