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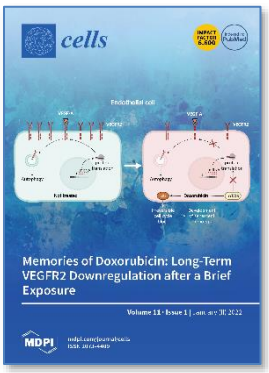

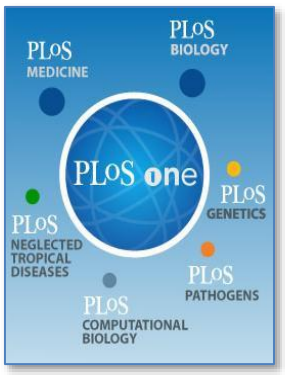

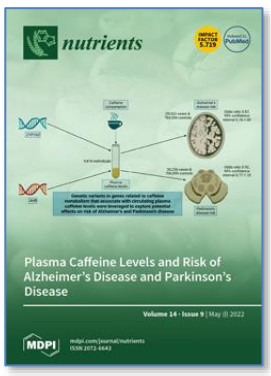

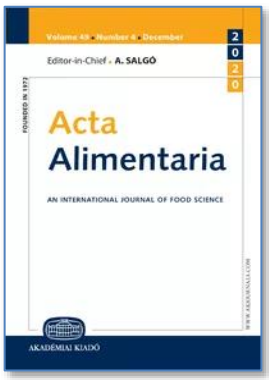

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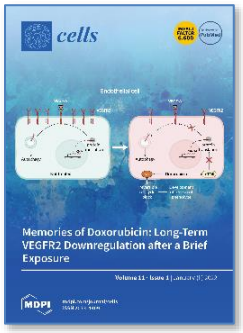
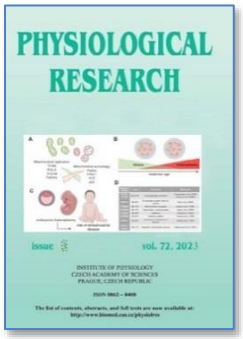
scientific publications and their abstracts

The journals in which the publications have appeared



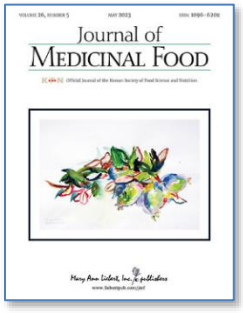
Cells:
Cells is an international, peer-reviewed, open access journal in cell biology, molecular biology and biophysics, published online bi-weekly by MDPI, and run by a prestigious group of editors who are currently active researchers and academics, as well as leaders in their fields. They also enjoy the support of an Editorial Advisory Board, reflecting all relevant segments of cell biology, including the newest emerging fields.



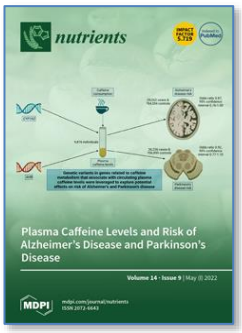
Physiological Research:
Physiological Research is a peer-reviewed, open access journal published online every two months by the Institute of Physiology - Czech Academy of Sciences. Published research findings help us understand how the human body works and how it adapts to environmental influences. It also helps us to identify the causes of disease, helping to develop new treatments and guidelines to maintain health.

Cancer Research:
The journal publishes studies and reviews that are of great importance to cancer research as a discipline. In addition, it seeks and publishes manuscripts that offer conceptual or technological advances that demonstrate new advances in translational processes in cancer biology. Particular attention is given to manuscripts that focus on convergence science, bridging two or more distinct areas of cancer research.

In Vivo:
In Vivo is an international, peer-reviewed journal that aims to bring together original, high-quality papers and reviews of experimental and clinical biomedical research in physiology, pathology and disease management. Topics covered include: development and application of diagnostic and therapeutic procedures; development of clinical trials and biomedical research models; diagnosis and treatment of cancer; immunotherapy and vaccines; regenerative medicine; carcinogenesis.



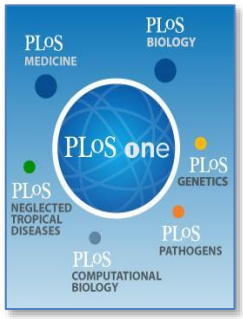
Journal of Medicinal Food:
The Journal of Medicinal Food is a monthly peer-reviewed medical journal founded in 1998. The journal focuses exclusively on the medicinal value and biomedical effects of foods (and their active ingredients). In addition, it develops internationally the knowledge of new foods and dietary supplements for health promotion and disease prevention and treatment.



Nutrients:
Nutrients is an open access, peer-reviewed scientific journal that publishes meta-analyses, regular research articles and short communications on all aspects of nutrition, usually twice a month. Founded in 2009 and published by the Multidisciplinary Digital Publishing Institute, the journal has an Impact Factor (IF) of 6,706 in 2023.

Acta Alimentaria International Journal of Food Science**:**
Acta Alimentaria publishes original publications and reviews on food science in the following disciplines: physics, physical chemistry, chemistry, analysis, biology, microbiology, enzymology, engineering, instrumentation, food automation and economics, food production and food technology, food quality, post-harvest treatments, food safety and nutrition.

Microchemical Journal:
Microchemical Journal is a peer-reviewed journal covering all aspects and phases of analytical chemistry, including sampling, sample preparation, measurement and data analysis. The *Microchemical Journal* publishes articles that are at the forefront of modern analytical chemistry, covering new technological innovations to the finest possible limits.



Plos One:
Plos One is an inclusive community of journals working together to promote the advancement of science for the benefit of society. It was founded to accelerate the pace and demonstrate the value of scientific progress. Their ars poetics: all scientific fields deserve regular publication and articles should be widely disseminated and freely accessible to all.

Europe PMC:
Europe PMC provides comprehensive access to life sciences literature from trusted sources. It is founded by the European Bioinformatics Institute (EMBL-EBI), an international, innovative and interdisciplinary research organisation dedicated to making the world's public biological data freely available to the scientific community. Europe PMC is a direct partner of PubMed Central (PMC).

ABOUT FLAVONOIDS - FLAVIN7 - FLAVIN77

The term flavonoid refers to a group of compounds whose members have a similar basic skeleton (flavone, isoflavone, etc.) to which OH (hydroxyl) and CH_3O (methoxy) groups are attached. These compounds occur partly free and partly in the form of glycosides (bound to carbohydrate components) in various plants.

István Rusznyák and Albert Szent-Györgyi

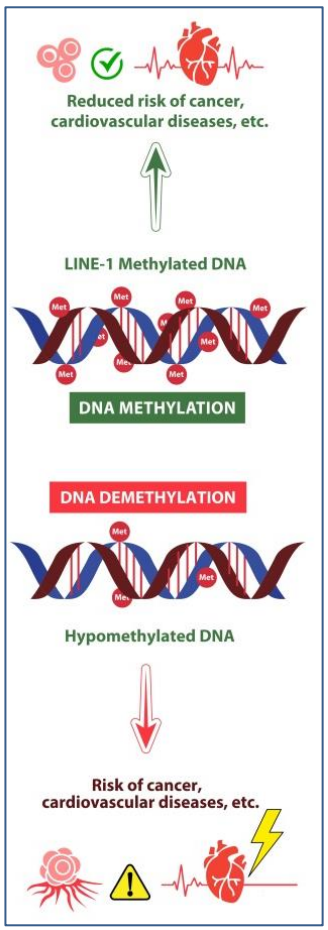
Flavonoids are mostly found in the skin and seeds of fruits. Rusznyák and Szent-Györgyi demonstrated in 1936 that they are produced in plants as essential immune substances and have vitamin-like effects in the human body. Other biological effects include antibacterial, hepatoprotective, anticancer and vascular support. With regard to the physiological effects of flavonoids, it is important to know that they act mainly in the digestive and circulatory systems. They inactivate free radicals and inhibit lipid peroxidation in the phospholipid layer of biomembranes, reducing the oxidised LDL ratio and thus reducing the risk of atherosclerosis. They prevent platelet aggregation and reduce thrombus formation. Increase the stability of vein walls. Their anti-tumour effect has been proven in thousands of studies (in vivo, in vitro), they help the utilisation of vitamin E, increase vitamin C and β-carotene levels, reduce serum triglyceride levels. Involved in arachidonic acid metabolism, anti-inflammatory. They reduce the long-term complications of diabetes and also have antiviral, antibacterial and antiallergic effects. Their pharmacological action lies, among other things, in the reduction of the transverse permeability of blood and capillaries, which is why they are successfully used in medicine for diseases related to capillary regulation (retinal and renal haemorrhage, etc.).

Another very frequently researched area of flavonoids is due to their suppressive properties on tumourigenesis. Malignantly transformed cells in different types of cancer share some common features, one of the most well-known of which is angiogenesis. This is not the fundamental cause of tumour growth but is essential for its development. One of the main directions of cancer research is to inhibit tumour angiogenesis, because when there is insufficient blood supply, the tumour "starves", its growth slows down or stops, and in favourable cases the process is reversed, i.e. the tumour cells die.

2022

Our state-of-the-art epigenetic studies track DNA methylation changes. The materials and methods used in these studies have been published for the first time in this context and are therefore a real novelty in scientific circles.

Effect of flavonoid extract, green tea extract, Japanese waxberry extract, coffee extract, olive oil and trans-fatty acid on DMBA-induced LINE-1 DNA methylation



A healthy diet and the use of appropriate biomarkers in early diagnosis are of paramount importance in prevention. Trans-fatty acids represent a major dietary risk, whereas many chemopreventive compounds have a protective effect on tumour biology, such as polyphenol-rich plant compounds or extra virgin olive oil, green tea, Japanese wax berries and coffee. A representative epigenetic biomarker of these factors is the methylation status of the promoter region of the Long Interspersed Element-1 (LINE-1) retrotransposon DNA segment.

The aim of the experiment was to determine how these carcinogenic/chemopreventive effects are reflected in the methylation patterns of LINE-1 DNA, to what extent the chemopreventive agents tested are able to prevent hypomethylation caused by DMBA, and whether these effects can be used as potential biomarkers. A further aim was to investigate the effect of trans-fatty acid on DMBA-induced LINE-1 DNA hypomethylation, whether it was able to enhance it or not.

In our study, we used eight groups of 12-week-old female CBA/Ca mice (n=6). Untreated control and DMBA-treated control groups received no pre-feeding, while one group of animals each received 4 mg/day/animal of green tea extract, 2.5 mg/day/animal of Japanese waxberry extract, 30 mg/day/animal of flavonoid extract, 30 mg/day/animal (150 ml) of coffee extract, 300 mg/day/animal of olive oil and 300 mg/day/animal of

trans-fatty acid for two weeks before DMBA treatment in addition to the usual diet. Except for the untreated (negative control) control group, the other seven groups received 20 mg/kg bw DMBA.
After 24 h of DMBA exposure, LINE-1 DNA methylation changes in liver, spleen and kidney were examined.

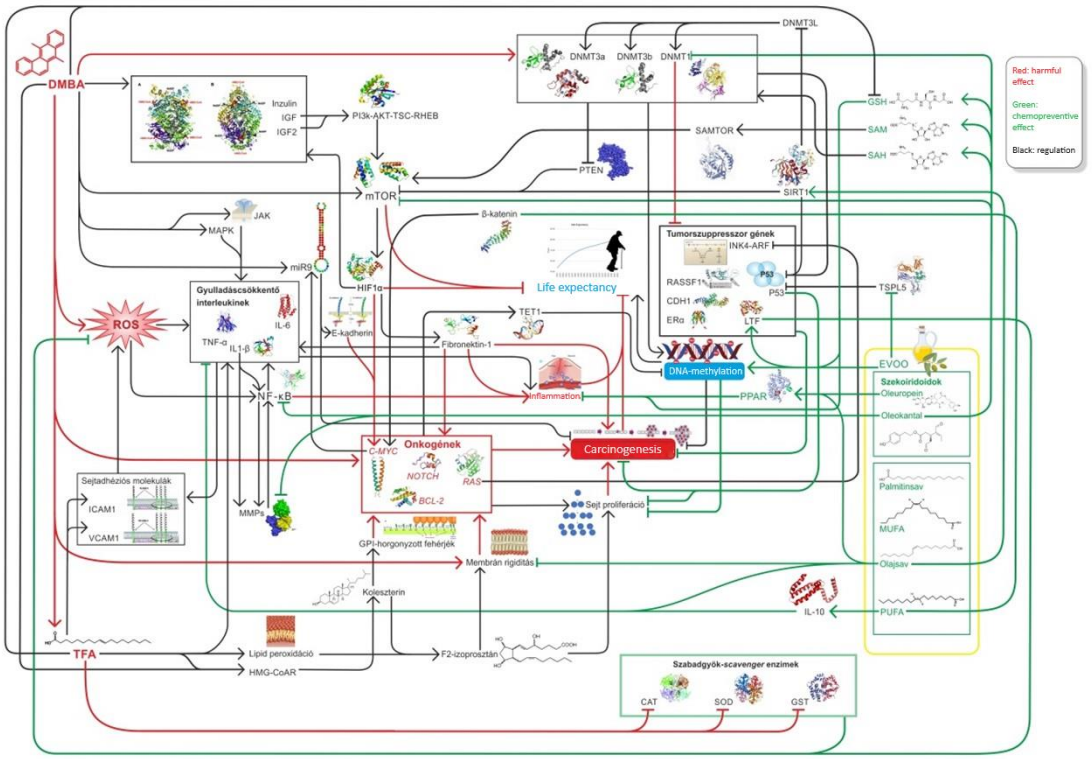


Figure 1: Summary of the molecular mechanisms and signalling processes affected by exposure to DMBA, TFA or EVOO (QR code for source designation).

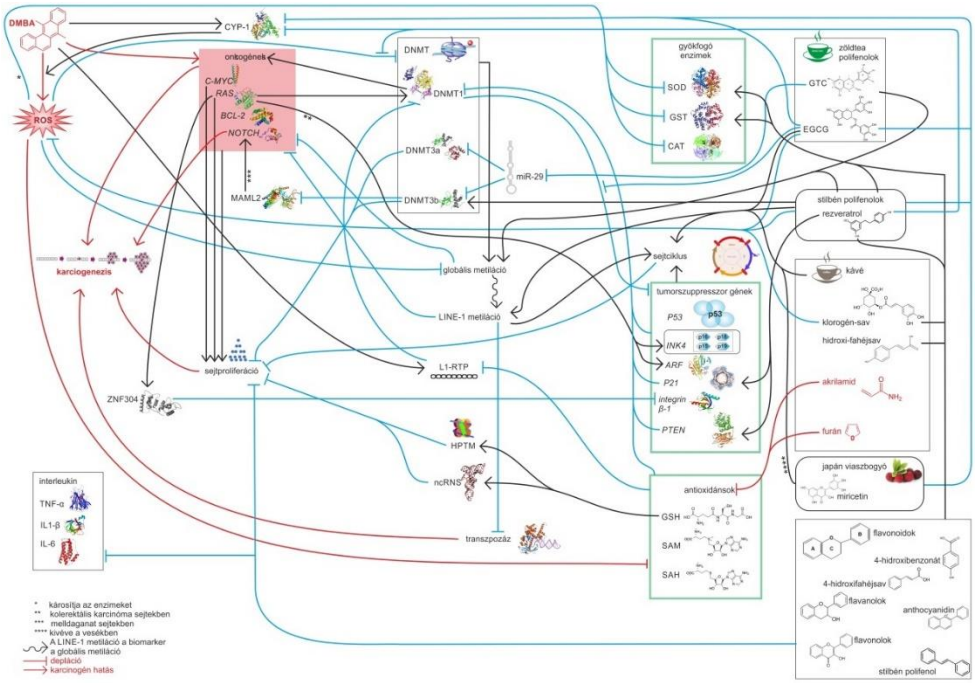
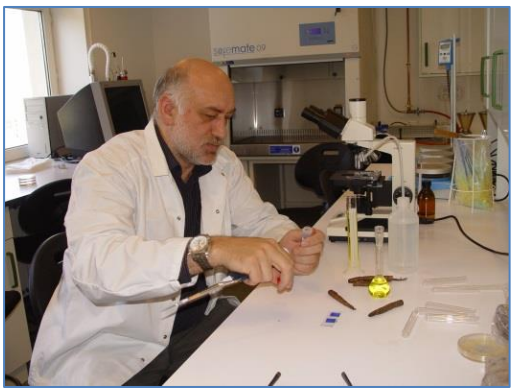


Figure 2: Summary of molecular mechanisms and signalling processes affected by exposure to DMBA, flavonoid extract, green tea extract, coffee extract or Japanese waxberry extract (QR code for source designation).



Dr. László Szabó PhD research epidemiologist

The DNA methylation changes we investigate may contribute to the anticarcinogenic and, in the case of TFA, carcinogenic effects of the chemopreventive agents under investigation, and are significantly representative of these processes as biomarkers. Furthermore, the LINE-1 DNA hypomethylation patterning assay system can be considered as a suitable molecular epidemiological biomarker for the investigation of the epigenetic effects of additional potentially chemopreventive agents.

Overall, flavonoid extract and green tea extract showed the strongest epigenetic protective effect, but coffee extract, olive oil and Japanese waxberry extract also showed protective effects. However, as expected, trans-fatty acid enhanced the antitumour effects.

Source: *Szabo L, Molnar R, Tomesz A, Deutsch A, Darago R, Varjas T, Ritter Z, Szentpeteri JL, Andreidesz K, Mathe D, Hegedüs I, Sik A, Budan F, Kiss I. Olive Oil Improves While Trans Fatty Acids Further Aggravate the Hypomethylation of LINE-1 Retrotransposon DNA in an Environmental Carcinogen Model. Nutrients. 2022 Feb 21;14(4):908. doi: 10.3390/nu14040908. PMID: 35215560; PMCID: PMC8878525.*
Full article: https://www.ncbi.nlm.nih.gov/pmc/articlesPMC8878525/

Szabo L, Molnar R, Tomesz A, Deutsch A, Darago R, Nowrasteh G, Varjas T, Nemeth B, Budan F, Kiss I. The effects of flavonoids, green tea polyphenols and coffee on DMBA induced LINE-1 DNA hypomethylation. PLoS One. 2021 Apr 20;16(4):e0250157. doi: 10.1371/journal.pone.0250157. PMID: 33878138; PMCID: PMC8057585.
Full article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8057585/

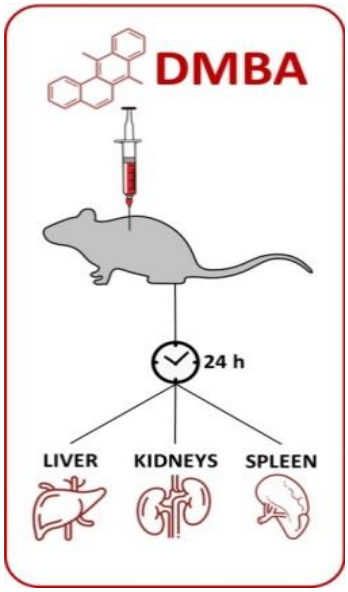
Figure 1

Figure 2

2022

We have developed an assay panel capable of detecting early signs of tumour development, thereby using a combination of proven carcinogens and putatively chemopreventive agents to identify anticancer agents.

Development of an early biomarker panel for the study of carcinogenic and chemopreventive agents based on gene expression and microRNA expression changes



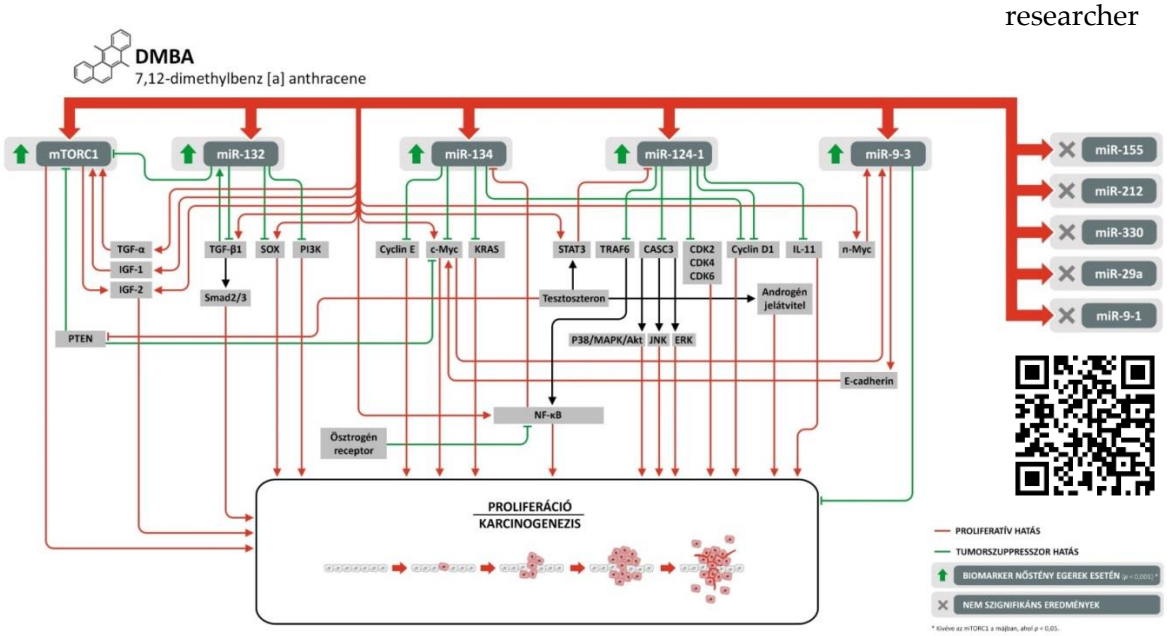
Due to the nature of cancer, prevention is of increasing importance in the fight against the development of the disease, where it is necessary to detect molecular biological phenomena indicating effects/damage caused by carcinogenic substances as early as possible, well before the onset of clinical symptoms.

Two groups of CBA/Ca mice were used in the study. Both the control and DMBA-treated groups -consisted of 12 (-68 weeks old) individuals (6 males, 6 females). The DMBA-treated group -received -20 mg/kg DMBA -dissolved in 0.1 ml of corn oil (Sigma-Aldrich, St. Louis, Missouri, USA) -intraperitoneally, -while the control group received 0.1 ml of corn oil alone. For both the negative control and treated groups, the -expression of -the miRNAs -and mTORC1 gene -tested were determined -24 h after DMBA treatment.

Overall, there is a -consistent and significant change in the mTORC1 gene and the miRNAs tested -(-miR91-, -miR93-, miR29a-, -miR1241-, miR132-, miR134-, miR155-, miR212-, miR330-), -statistically significant and in the same direction in all organs tested, -was observed for miR134-, miR132-, -miR1241-, -miR93 -miRNAs -and the mTORC1 gene in female mice.- These important test criteria were less fulfilled for the other miRNAs or in general in the organs of the male animals tested. The design of the test panel in our study was based on the inclusion of these miRNAs and the mTORC1 gene.

The complexity of the molecular processes of carcinogenesis requires the extension of test systems to the widest possible range of signalling pathways and their regulators. The miR-9-3, miR-124-1, miR-132 and miR-134 miRNAs and the mTORC1 gene are involved in signalling pathways such as RAS/MAPK/ERK, RAS/PI3K/AKT, p38 MAPK, or JNK, which typically show higher activity already in the early phase of carcinogenesis.

Dr. András Tomesz PhD researcher



Applied in practice, the 5 biomarker-based assay panel designed to predict carcinogenesis could be a valuable tool for further investigation, detection of carcinogen exposures, and detection of tumour suppressor compounds for chemoprevention and/or complementary therapy, thus opening up new opportunities for reducing tumour incidence and mortality by using it as a tool for primary, secondary and tertiary prevention.

Source: *Tomesz A, Szabo L, Molnar R, Deutsch A, Darago R, Raposa BL, Ghodratollah N, Varjas T, Nemeth B, Orsos Z, Pozsgai E, Szentpeteri JL, Budan F, Kiss I. Changes in miR-124-1, miR-212, miR-132, miR-134, and miR-155 Expression Patterns after 7,12-Dimethylbenz(a)anthracene Treatment in CBA/Ca Mice. Cells. 2022 Mar 17;11(6):1020. doi: 10.3390/cells11061020. PMID: 35326471; PMCID: PMC8947631.*

Full article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8947631/

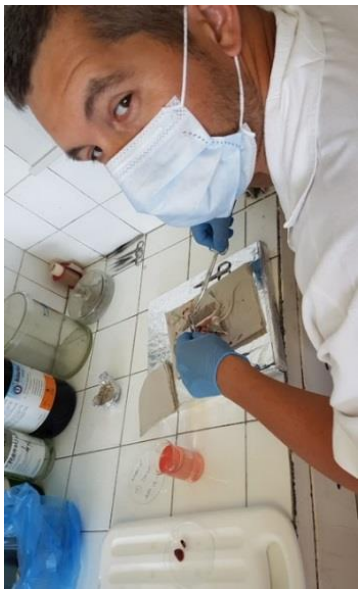
Tomesz A, Szabo L, Molnar R, Deutsch A, Darago R, Mathe D, Budan F, Ghodratollah N, Varjas T, Nemeth B, Kiss I. Effect of 7,12-Dimethylbenz(α)anthracene on the Expression of miR-330, miR-29a, miR-9-1, miR-9-3 and the mTORC1 Gene in CBA/Ca Mice. In Vivo. 2020 Sep-Oct;34(5):2337-2343. doi: 10.21873/invivo.12046. PMID: 32871758; PMCID: PMC7652467.

Full article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7652467/

2022

Applying in practice the test panel described above, we examined six substances found in the human diet, olive oil, green tea, Japanese waxberry extract, flavonoid complex, coffee extract and trans-fatty acid, with the aim of understanding their potential protective or harmful effects on tumour development.

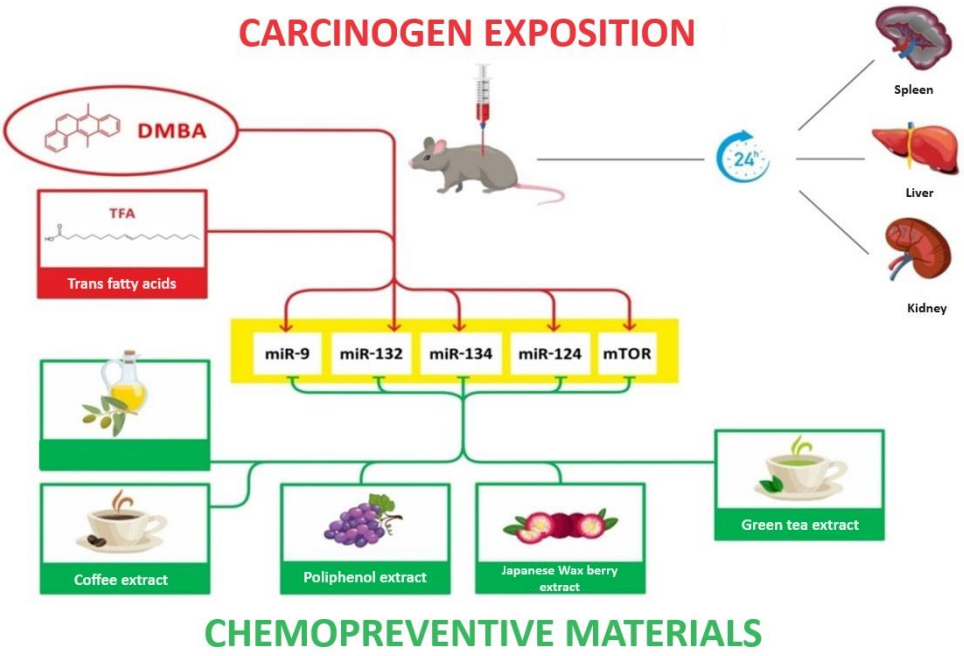
Effects of olive oil, coffee extract, Japanese waxberry extract, green tea extract, polyphenol extract and trans-fatty acids on miR-134, miR-132, miR-124-1, miR-9-3 and mTORC1 gene expression in vivo in DMBA-treated mice



Dr. Richárd Molnár
PhD
researcher,
epidemiologist

Epidemiological studies have shown that chemopreventive polyphenols reduce the chance of tumour formation. Among these, flavonoids are particularly promising chemopreventive agents. Accordingly, in our studies we tested the chemopreventive effects of extra virgin olive oil, green tea, Japanese wax berry, coffee and a polyphenol extract, as well as the putative harmful effects of trans-fatty acid.
In our study, we used 6-8 week old female CBA/Ca mice, housed in separate cages per group. Groups of animals (n=6) were fed olive oil at a dose of 300 mg/animal per day, trans-fatty acid also at a dose of 300 mg/animal per day, green tea extract at a dose of 4 mg/animal per day, Japanese waxberry extract at a dose of 2.5 mg/animal per day, polyphenol extract at a dose of 30 mg/animal per day and coffee extract at a dose of 30 mg/animal (150 ml) per day mixed with their diet for 14 days. The above groups were treated intraperitoneally (i.p.) with 20 mg DMBA per kg body weight dissolved in 0,1 ml corn oil. In addition, a positive control group (n=6) was administered DMBA alone as mentioned above. 24 h after DMBA exposure, we examined the changes in

expression of miR-134, miR-132, miR-124-1, miR-9-3 and mTORC1 gene as biomarkers in the liver, kidney and spleen of the animals.



Our results suggest that polyphenol extract, green tea extract, Japanese waxberry extract, extra virgin olive oil, and coffee extract inhibit tumor development through increasing epigenetic changes induced by DMBA, while trans-fatty acid promotes it.

Source: *Molnar R, Szabo L, Tomesz A, Deutsch A, Darago R, Raposa BL, Ghodratollah N, Varjas T, Nemeth B, Orsos Z, Pozsgai E, Szentpeteri JL, Budan F, Kiss I. The Chemopreventive Effects of Polyphenols and Coffee, Based upon a DMBA Mouse Model with microRNA and mTOR Gene Expression Biomarkers. 2022 Apr 12;11(8):1300. doi: 10.3390/cells11081300. PMID: 35455979; PMCID: PMC9029301.*
Full article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9029301/
Molnar R, Szabo L, Tomesz A, Deutsch A, Darago R, Ghodratollah N, Varjas T, Nemeth B, Budan F, Kiss I. In vivo effects of olive oil and trans-fatty acids on miR-134, miR-132, miR-124-1, miR-9-3 and mTORC1 gene expression in a DMBA-treated mouse model. PLoS One. 2021 Feb 4;16(2):e0246022. doi: 10.1371/journal.pone.0246022. PMID: 33539381; PMCID: PMC7861522.
Full article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7861522/

Studies on Flavin7 and Flavin77 high bioflavonoid preparations

Tumours share many common characteristics, one of the best known being that cell proliferation is continuous, uncontrolled, and in a sense infinite, unless some external intervention is made. A good example of this is the following study, in which Slovak researchers investigated the tumour suppressive (angiogenesis suppression and antiproliferation) effects of Flavin7 products in 2008.

The Flavin7 formulation contained extracts of seven types of red fruits. Its polyphenol content was far below that of the current Flavin77 Cyclo Cyto formulations, but it still showed significant results in health protection.

University of Pécs
Faculty of General Medicine

University of Debrecen
Faculty of Medicine

Semmelweis University

2016

Consumption of Flavin7 can have a significant anti-tumour effect in breast cancer.

Polyphenols from fruit peel show significant antitumor activity in a breast cancer model - (N-methyl-N-nitrosourea, mammary carcinogenesis, in female rats)

Fruit and vegetable intake is inversely correlated with cancer, so evidence suggests that phytochemical extracts present in fruits, vegetables or cereals may have anti-cancer effects. Therefore, the antitumor effect of Flavin7 was modeled in the chemoprevention of N-methyl-N-nitrosourea-induced mammary carcinogenesis in female rats.

Methods: Two concentrations of Flavin7 lyophilized material, 0.3 and 3%, were administered to the animals in medium. The experiment was terminated 14 weeks after carcinogen administration, mammary tumours were removed and prepared for histopathological and immunohistochemical analysis. In addition, we performed apoptosis and proliferation assays in human mammary adenocarcinoma (MCF-7) cells after F7 treatment by in vitro cytotoxicity assay.

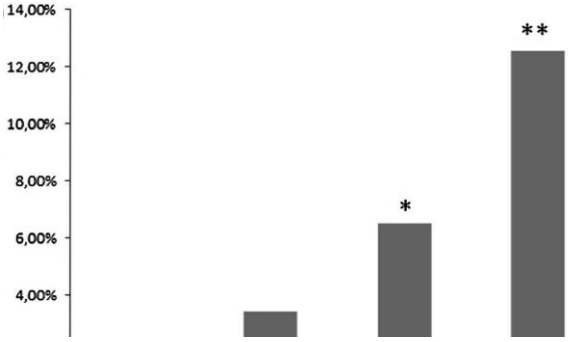


Figure 1: Flavin7 dose-dependently increased the apoptotic intensity of tumour cells, i.e. reduced tumour size. Y-axis: Apoptotic index (%)

RESULTS: High-dose F7 reduced tumor incidence by 58% ($p<0.001$), tumor incidence by 24% ($p<0.05$), and prolonged latency by 8 days ($p<0.05$) compared to control rats, while lower-dose F7 was less effective. Histopathological analysis of tumours showed a significant reduction in the proportion of high/low grade carcinomas after high dose F7 treatment. In vivo immunohistochemical analysis of rat carcinoma cells found a significant increase in caspase-3 expression and a significant decrease in Bcl-2, Ki67 and VEGFR-2 expression in the high dose group. Both doses showed a significant positive effect on plasma lipid metabolism in rats. F7 significantly decreased the survival of MCF-7 cells in in vitro MTT assay in a dose- and time-dependent manner compared to the control. F7 prevented cell cycle progression by significantly enriching G1 cell

populations. Incubation with F7 showed a significant increase in the percentage of annexin V-/PI-positive MCF-7 cells and DNA fragmentation.

Conclusions: Our results show a significant tumour suppressive effect of Flavin7 in the breast cancer model. We find that the effects of phytochemicals present in the fruit extract are responsible for the strong anticancer effects observed.

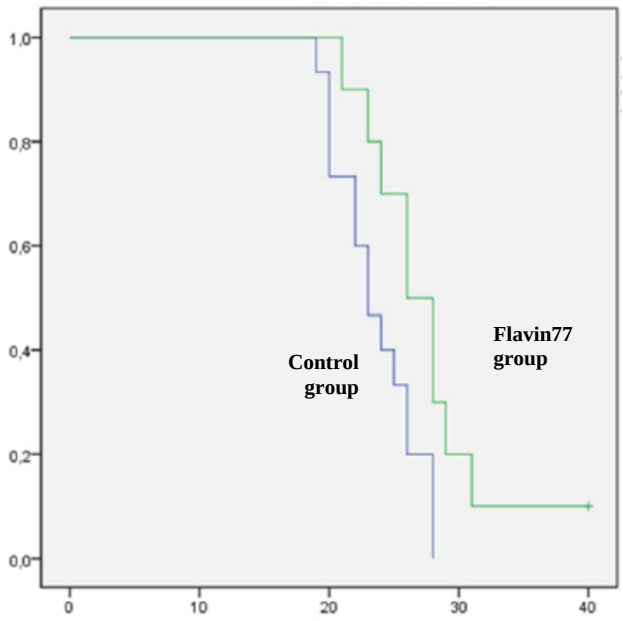
Source: *Kubatka P, et al. Fruit peel polyphenols demonstrate substantial anti-tumour effects in the model of breast cancer. Eur J Nutr. 2016 Apr;55(3):955-65. doi: 10.1007/s00394-015-0910-5. PMID: 25930965.*

2012

Flavin77 consumption inhibited B16 melanoma tumor growth compared to the control group, an effect also observed in early biomarkers (miRNAs).

Effect of flavonoid-containing dietary supplementation on miRNA expression in mice inoculated with B16 melanoma

Melanoma malignum is one of the least common and most deadly types of skin cancer, but it is also one of the easiest cancers to detect, screen for and prevent. If melanoma is detected early and surgical removal of the tumour is possible, the chances of a complete cure are high, but late detection and diagnosis reduces the chances of successful treatment and cure. Everyone has some risk of melanoma, but the increased risk depends on the following main factors: sun exposure, number of moles on the skin, skin type and family history (genetics).



The ever-expanding range of chemopreventive compounds provides us with a variety of antioxidant combinations. The protective effects of antioxidant supplements are widely accepted and proven for different types of cancer, but their use in the prevention of melanoma is not yet fully understood.

In the present study, we investigated the effects of a high flavonoid antioxidant preparation (Flavin77, which was tested as FEMADN2 according to the study protocols) in male C57BL/6N mice inoculated with B16 mouse melanoma.

We analysed the expression profiles of 12 miRNAs from liver, spleen, lung and kidney of animals and from transplanted melanoma tissues.

Flavin77, a systemic multicomponent antioxidant compound, had an observable effect on tumour growth and induced significant changes in miRNA expression in vital organs.

Source: *Wolher, V ; Gombos, K ; Juhász, K ; Gőcze, K ; Kiss, I ; Tibold, A ; Szabó, L ; Sebestyén, A ; Huszár, A ; Németh, Á et al. Effect of flavonoid-containing dietary supplementation on miRNA expression in mice inoculated with B16 melanoma MAGYAR EPIDEMIOLOGIA 9 : 2 pp. 139-149. , 11 p. (2012)*

2009

Flavin7 treatment has bronchodilator and anti-inflammatory effects on allergic airway inflammation.

Effect of Flavin7 on allergen-induced airway hyperreactivity

Abstract: Some studies have suggested that polyphenol compounds may reduce the incidence of asthma symptoms.

The aim of our experiments was to evaluate the effect of 21 days of Flavin7 flavonoid administration on experimentally induced airway inflammation in guinea pigs sensitized to ovalbumin (OVA).

We investigated tracheal smooth muscle reactivity by in vitro isovelocity method; changes in airway resistance by in vivo plethysmography; histological imaging of tracheal tissue; and levels of interleukin 4 (IL-4) and interleukin 5 (IL-5) in bronchoalveolar lavage fluid (BALF). The histopathology of tracheal tissue and the concentrations of the inflammatory cytokines IL-4 and IL-5 in BALF were used as an index of airway inflammation.

Administration of Flavin7 caused a significant reduction in specific airway resistance following histamine challenge and a reduction in tracheal smooth muscle contraction amplitude in response to bronchoconstrictor mediators.

Flavin7 minimized the extent of inflammation estimated from eosinophil counting and IL-4 and IL-5 concentrations.

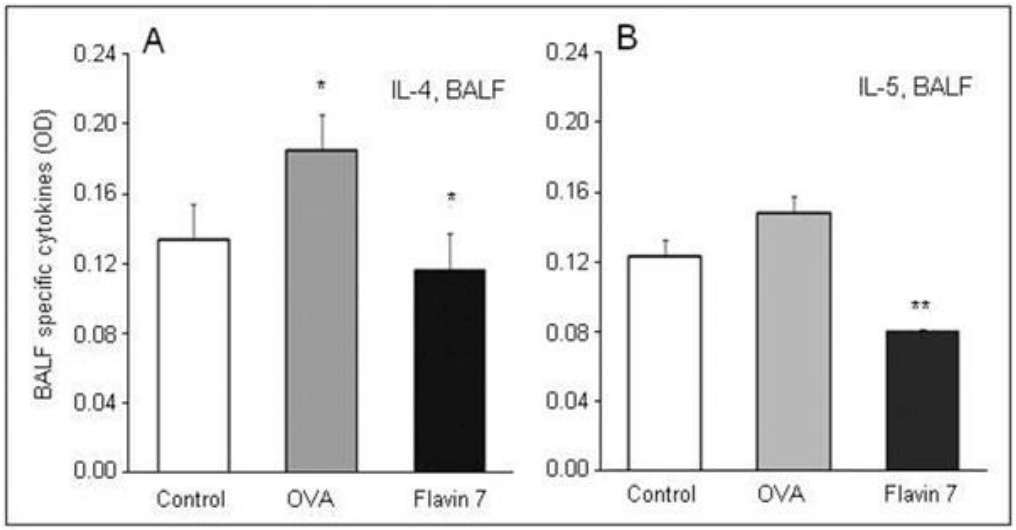


Figure 1: Comparison of IL-4 (panel A) and IL-5 (panel B) inflammatory cytokine levels in BALF of control, OVA-sensitized and OVA-sensitized guinea pigs treated with Flavin7. Data are means ± SE; n = 10 in each group; *p<0.05.

In conclusion, Flavin7 administration showed bronchodilator and anti-inflammatory effects on allergen-induced airway inflammation.

Source: *Franova S, Joskova M, Novakova E, Adamicova K, Sutovska M, Nosal S. Effects of flavin7 on allergen induced hyperreactivity of airways. Eur J Med Res. 2009 Dec 7;14 Suppl 4(Suppl 4):78-81. doi: 10.1186/2047-783x-14-s4-78. PMID: 20156731; PMCID: PMC3521342.*

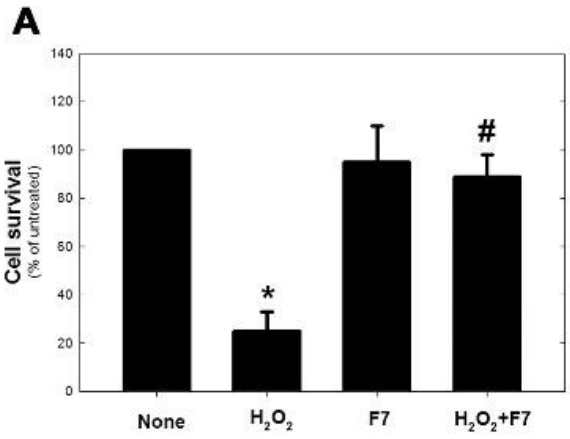
2009

Flavin7 supplementation may be beneficial for cancer patients to prevent oxidative stress kidney toxicity associated with anticancer drugs or cancer progression.

Plant-derived natural compound Flavin7 reduces oxidative stress in renal proximal tubule cells (in vitro)

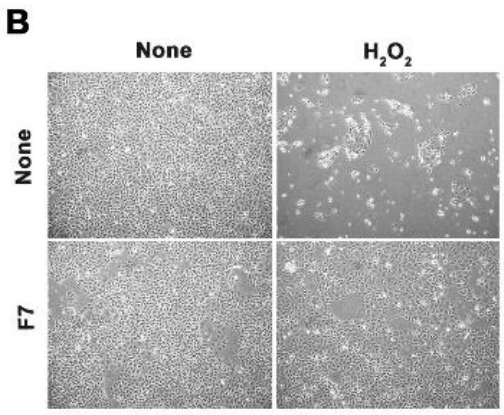
Cancer therapies and cancer progression can increase oxidative stress, which can cause kidney toxicity in cancer patients. Flavin7 is a natural polyphenol-containing dietary supplement with potential antioxidant activity. It may therefore help to reduce the renal toxicity of chemotherapeutic agents.

Materials and Methods: Cultured mouse renal proximal tubule cells were subjected to $H O_{22}$ mediated oxidative stress. The potential antioxidant effects of Flavin7 were assessed by measuring reactive oxygen species (ROS) production, mitochondrial depolarization and injury (lactate dehydrogenase release and tryptic exclusion) in cells pretreated with F7 before $H O_{22}$ treatment.



RESULTS: Flavin7 pretreatment significantly reduced $H O_{22}$ -induced ROS production, mitochondrial depolarization and consequent damage in renal proximal tubules.

CONCLUSION: These results show that hydrogen peroxide-induced ROS production was reduced by Flavin7, and in addition, ROS production was not inhibited at all in the Flavin7 pretreated group. It is clear that Flavin7, with its high polyphenol content, is



able to inhibit hydrogen peroxide-induced cytotoxicity and the resulting apoptosis.

This study demonstrates that the use of Flavin7 in cancer therapy improves patients' chances of survival.

Source: *Ember A, Clark JS, Varjas T, Kiss I, Ember I, Baliga R, Arany I. The plant-derived natural compound flavin 7 attenuates oxidative stress in cultured renal proximal tubule cells. In Vivo. 2009 Nov-Dec;23(6):975-8. PMID: 20023242.*

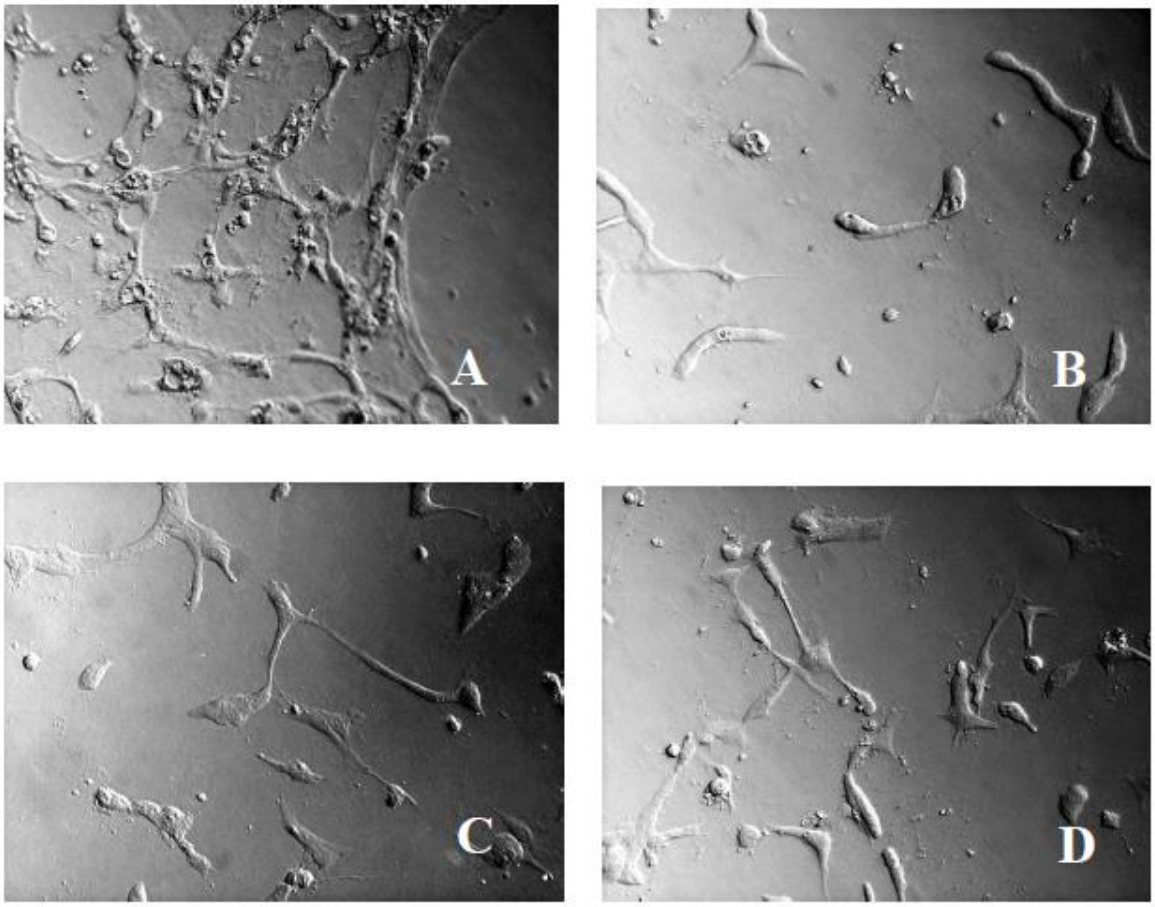
2008

"We concluded that Flavin7 is antiproliferative, and its anti-angiogenic effect can effectively suppress the development of cancer." - Prof. J. Mojzis, Head of Research.

In vitro antiproliferative and antiangiogenic effects of Flavin7

Abstract: Flavin7 is a dietary supplement commonly taken by cancer patients in Central Europe during chemotherapy and radiotherapy. In this study, we investigated the antiproliferative and antiangiogenic effects of this supplement. Flavin7 showed antiproliferative activity in Jurkat and HeLa cells. It significantly reduced the growth of both cancer cell lines at a dose of 200 μg/ml to 20 μg/ml ($p<0.001$ and $p<0.01$, respectively). In F7-treated Jurkat cells, we observed a significant increase in the sub-G(0)/G(1) DNA-containing cell fraction, which is considered as a marker of apoptotic cell death. Apoptosis was confirmed by annexin V staining and DNA fragmentation. Furthermore, Flavin7 at doses ranging from 100 μg/ml to 4 μg/ml inhibited endothelial cell migration and capillary tube formation, suggesting that it has potential anti-angiogenic properties. Flavin7 also inhibited the activity of matrix metalloproteinases (MMPs), mainly MMP-9 at doses ranging from 100 μg/ml to 4 μg/ml. Our data suggest that Flavin7 has pronounced antiproliferative and antiangiogenic properties in vitro. Further studies are needed to clarify the in vivo activities.

Flavin7 blocked the development of new blood vessels in a dose-dependent manner, thereby inhibiting the formation of the nutrient pathways, or capillaries, necessary for tumour growth.
In the picture: without Flavin7 (A), 20 μg/ml (B), 10 μg/ml (C) or 4 μg/ml (D). Inhibition of human endothelial cell capillaryization was achieved with the 20 μg/ml (B) treatment. It can be shown that the formation of new blood vessels necessary for tumour growth can be stopped by Flavin7 administration, thereby reducing and reversing tumour growth.



"We observed significant in vitro suppressive effects of Flavin7 on the growth, cell cycle and apoptosis of human tumour cell lines. We also identified additional mechanisms such as effects on growth, migration, endothelial cell 'capillary' formation and inhibition of MMPs. We conclude that the antiproliferative and anti-angiogenic effects of Flavin7 can effectively suppress cancer development" - Prof. J. Mojzis, Head of Research

Source: *Mojzis J, Sarisský M, Pilátová M, Voharová V, Varinská L, Mojzisová G, Ostro A, Urdzík P, Dankovcik R, Mirossay L. In vitro antiproliferative and antiangiogenic effects of Flavin7. Physiol Res. 2008;57(3):413-420. doi: 10.33549/physiolres.931127. PMID: 18597584. http://www.biomed.cas.cz/physiolres/pdf/57/57_413.pdf*

2007

Consumption of Flavin77 helps the body to fight against tumours such as kidney tumours or liver tumours, which are more powerful when used as a preventive measure before the tumour develops.

High phytochemical content
Anti-cancer effects of Flavin77 plant extract

In recent years, a number of phytochemicals from plants have been shown to have cancer-preventing or anti-cancer effects. These compounds may also have a place in cancer therapy, of course not as a substitute for chemo- or radiotherapy, but as a way of enhancing the effectiveness of standard therapeutic methods. The potential anti-cancer effects of a plant extract (Flavin77, a dietary supplement containing high levels of flavonoids and other phytochemicals) were investigated in an animal

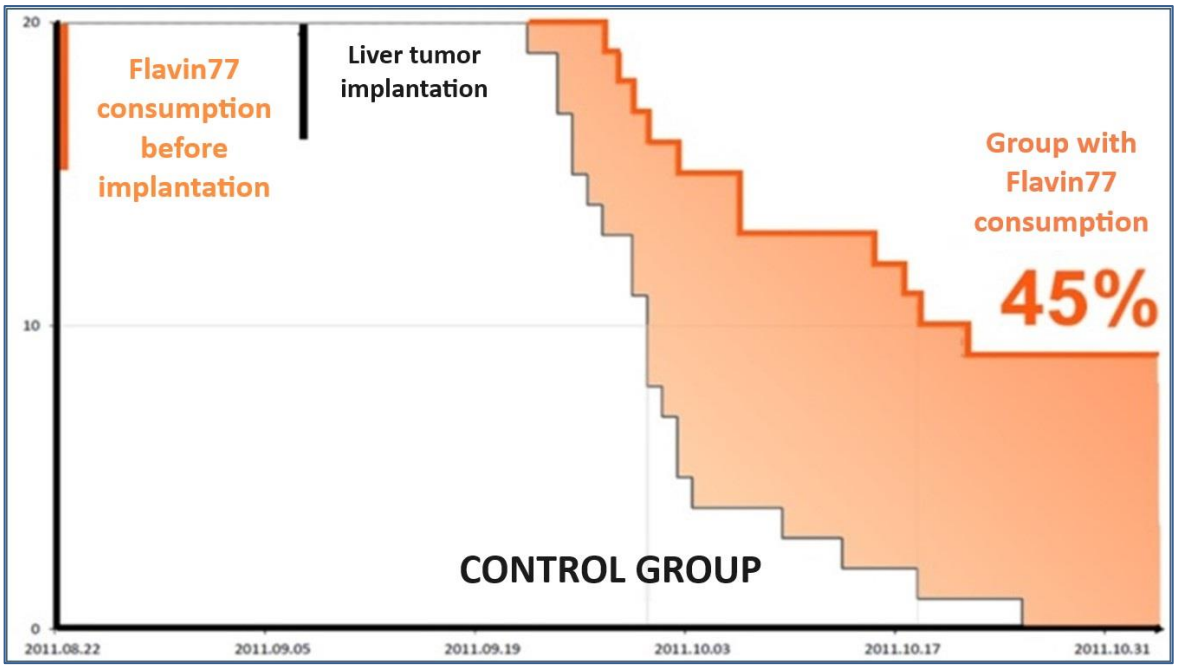


Figure 1: The survival of the Flavin77 group was 45% at the end of the observation period, while the control group died completely in almost 3 months.

model.

F344 rats (6-8 weeks old, 12/group) were injected with $5x10^5$ hypernephroma cells under the dorsal skin. The animals received Flavin77 in their drinking water at a

body weight equivalent dose according to the recommended human recommendation starting from the day of tumour transplantation. In another group, we performed a preventive 14-day pre-infusion with the same dose, then injected $5x10^5$ He/De liver tumor cells under the kidneys and continued Flavin77 supplementation.

Flavin77 treatment significantly increased the survival of animals with renal tumours. The median survival was 41.5 days in the treated group compared to 30 days in the controls, $p<0.05$, with the longest survival being 52 days in the Flavin77 group and 47 days in the control group. In addition, we observed significant results in the survival of animals with liver tumours.

Our results suggest that flavonoid-containing plant extracts may play a role in the therapy of the tumour types studied, as they have anti-cancer effects in animal models

Source: *Zs. Orsós, L. Szabó, K. Gombos, I. Ember, I. Kiss. Emirates Medical Journal. Vol. 25. (1): 78. 2007*.

2007

Flavin7 treatment is able to inhibit the progression of malignant renal tumours by affecting several intracellular pathways

Effect of a plant-derived natural compound, Flavin7, on the ERK signaling pathway in immortalized mouse proximal tubule cells

Abstract: As MAP kinases represent an important pathway for the translation of external stimuli into internal signals in cells, identifying their potential role in cancer cells may be a promising method for the treatment and prognosis of malignancies. Our previous experiments have shown that Flavin7, a flavonoid-rich solution, was able to reduce renal tumour growth in vivo.

MATERIALS AND METHODS: The effect of Flavin7 on the MAPK signaling pathway was determined in immortalized mouse proximal tubule cells by cell viability assay, flow cytometry analysis, luciferase assay and Western blot.

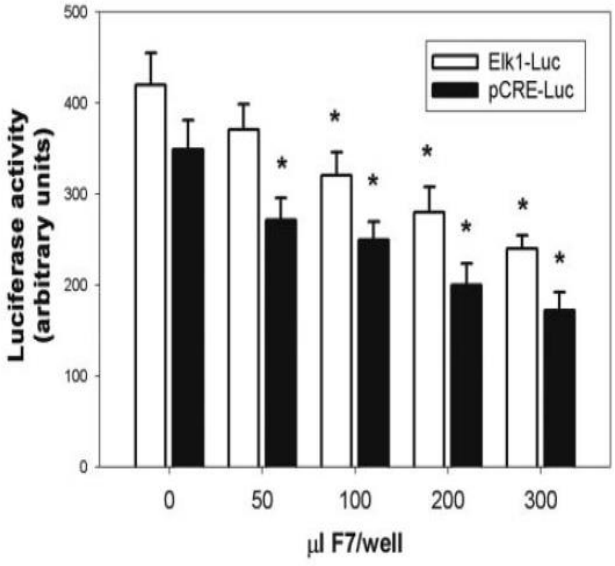


Figure 1: Effect of F7 on the downstream function of ERK. Renal cancer cells were transiently transfected with the pFR-Luc reporter plus pFA2-Elk1 trans-activator plasmid and a '-galactosidase plasmid (open lanes) or a pCRE-Luc plus '-galactosidase plasmid (filled lanes) as described in the Materials and methods section. After 24 h, cells were treated with F7 for 12 h and luciferase activity was determined together with '-galactosidase activity. Luciferase activity was calculated as the ratio of luciferase activity normalized by '-galactosidase activity (mean±S.D.,n=3; *$p<0.001$ compared to untreated control).

RESULTS: Flavin7 significantly reduced ERK phosphorylation and inhibited downstream targets such as Elk1 and CREB activity by suppressing ERK kinase MEK1.

Conclusion: Given its ability to temporarily inhibit renal tumor growth and activation of the MEK1/ERK pathway in vitro, further in vivo studies may determine the potential role of Flavin7 in the treatment of malignancies.

Source: *Nádasi E, Ember I, Arany I. Effect of a plant-derived natural compound, Flavin7, on the ERK signaling pathway in immortalized mouse proximal tubule cells. In Vivo. 2007 Sep-Oct;21(5):871-5. PMID: 18019427.*

2002

Unfortunately, in the field of oncology and cardiology, the therapeutic methods used by the official clinic often do not bring the expected cure and recovery. However, Flavin7 treatment, which is considered complementary medicine, has significantly improved patients' chances of survival.

Bioflavonoids and oncological care
Clinical experience with Flavin7

Sándor Erdős, László Szabó
County Hospital Oncology Nagykanizsa
"Flavin for health!" Public Benefit Social Foundation Eger

Goal: To improve the prevention of malignant cancer and the quality of life of patients receiving treatment and rehabilitation care. To monitor clinical status during the administration of Flavin7, a dietary supplement containing a high level of bioflavonoids, and to follow the progression of the disease and changes in the disease process, with particular attention to the quality of life.

Dr. Sándor Erdős †
oncologist

Methods: a multicentre, randomised controlled clinical trial of volunteer patients and physicians, which is a non-substitute for the Flavin7 treatment strategy of academic medicine. 33 physicians completed a clinical trial of 295 patients.

Results: Flavin7 is a dietary supplement containing bioflavonoids, resveratrol, anthocyanins, vitamins and minerals, trace elements. Its oxidative radical scavenging activity is concentration and time dependent, exceeding similar characteristics of commercially available formulations. Flavin7 inhibits tumour proliferation, improves the quality of life of patients, reduces or prevents the side effects of chemo- and irradiation therapy. It has hepatoprotective and cardiotoxicity-protective effects. Reduces pain caused by osseous metastases. Improvement in psychological well-being and alleviation of depressive symptoms have been observed by our clinicians.

Conclusions: International scientific literature references and epidemiological data suggest a major role for bioflavonoids in prevention. To date, scientifically proven

treatment methods have failed to improve patients' quality of life, survival, complete and partial remission to the expected extent. Flavin7 given as an adjunctive treatment has significantly improved patients' quality of life, complete and partial remission rates. Clinical observations suggest that the widespread use of bioflavonoids can substantially reduce cardiovascular and malignant cancer morbidity and mortality, and improve the outcome of chemoprevention. An extended clinical trial in accordance with the requirements of the national scientific community is considered justified.

"A paradigm shift is needed in all areas of oncology care, and we recommend the inclusion of Flavin7 in chemoprevention and oncology treatment protocols. Complementary therapies should not be categorically rejected, especially if they are in the best interest of the patient's recovery." - Dr Sándor Erdős

Source *: http://slomanut.freevar.com/literatura/the_use_of_bioflavonoides_in_oncology%5B1%5D.pdf*

2001

The world-leading mortality figures for malignancies in Hungary necessarily demand the introduction of new prophylactic methods, devices and curative procedures in addition to the official conventional medical treatment methods.

The role of flavonoids in maintaining health and curing cancer

In the years preceding the millennium, and again in 2001, scientific publications on antioxidants, flavonoids, resveratrol, in addition to arteriosclerosis and diseases of the heart and circulatory system, mainly covered malignant tumours. Noteworthy is a statement published in December 1997 by the International Agency for Research on Cancer (IARC) in Lyon, France, which concluded that the risk of cancer is undoubtedly lower in populations with a high intake of fruit and vegetables. However, no conclusive evidence has been found that any one component of the food consumed has a cancer-preventive effect in itself.

"(...) Over time, the role of natural supplements in cancer prophylaxis has increased. Recent scientific publications on flavonoids, resveratrol have confirmed the free radical inhibitory properties of these natural plant substances, the reduction of oxidative stress, their antimitotic effect in carcinogenesis."

Resveratrol is a natural plant immune substance, its effects include inhibiting tumour cell proliferation, metastasis and anti-angiogenesis of neovascularisation. Resveratrol induces apoptosis and reduces mitotic activity in human tumour cells, as reported by domestic authors. Resveratrol and quercetin are effective in inhibiting the growth and proliferation of oral squamous cell carcinomas and are therefore considered to be an effective tool for chemoprevention. In human breast cancer cells, resveratrol inhibits COX-2 transcription. Our studies confirm the anti-cancer anti-inflammatory effects of resveratrol. Apigenin and quercetin, belonging to the flavonoid group, inhibit melanoma growth and invasiveness, and their inclusion in therapeutic protocols is therefore considered justified. Quercetin inhibits P21-RAS expression in primary human colon carcinoma cell lines. It is thought to have a chemopreventive role in colorectal carcinogenesis. The antiangiogenic effect of silymarin has also been described, inhibiting lipid peroxidation, preventing cell membrane damage through

its antiperoxidative, free radical scavenging properties. In the nucleus, it enhances the synthesis of ribosomal RNA through the activity of RNA polymerase 1.

The world-leading mortality data on malignant tumours in Hungary necessarily call for the introduction of new prophylactic methods, tools and therapeutic procedures in addition to the official conventional medical treatment methods, not separated from the application of scientific naturopathic complementary, holistic medicine. The complementary treatment of cancer by natural therapies is now accepted in Western medicine. The administration of mistletoe and thymus extracts, cellular and peptide therapy, enzyme therapy, phytotherapy, symbiosis management, intestinal bacterial flora regulation, topical and whole-body hyperthermia, orthomolecular treatment - antioxidant administration, complementary treatment based on empirical clinical observation and evidence, are all essential in the everyday management of cancer patients.

The guiding principle of "nil nocere" (do no harm) and "salus aegroti suprema lex" (the patient's welfare is the supreme law) can guide our healing activities. The positive scientific references to flavonoids and resveratrol in general as antioxidants have attracted our interest in their use in cancer patients.

Chance has also come to our rescue, because in our chemotherapy practice we have observed in some patients that the side effects of aggressive chemotherapy - stomatitis, mucositis, vomiting, diarrhoea, allopecia, depression - were significantly reduced or absent. As it turned out, these patients were taking capsules containing flavonoids and vitamin E.

The scientifically proven effects of flavonoids are antitumour, mitosis and mutation inhibition, anti-atherosclerotic, anti-inflammatory, antiviral and anti-allergic. Inhibit LDL oxidation, reduce cardiovascular catastrophes, platelet aggregation. In search of a domestic product, we came across the formulation containing flavonoids, anticyanides, resveratrol and other antioxidants developed by László Szabó and his colleagues. Flavin7 is a non-medicinal nutritional supplement, a molecularly separated concentrate of fruit extracts collected from areas protected from environmental damage, selected according to place of production and variety. In addition to resveratrol, Flavin7 contains 12 flavonoids, including chrysin, galangin, apigenin, luteolin, valerol, quercetin, hesperidin and anticyanidins. As a fruit concentrate it also contains vitamins, trace elements and minerals.

Clinical experience with Flavin-7: Clinical observations have been made in more than 20 patients, mainly with breast cancer, gastrointestinal, gastric and colorectal cancer. According to the professional rules of patient follow-up, in addition to physical examinations, laboratory parameters, tumor markers, staging tests, diagnostic imaging techniques were used with thorough anamnesis, analysis and quality of life analysis. These data were included in patient records. It should be emphasised that the therapeutic methods of modern academic medicine (surgical, irradiation, drugs, cytostatic, hormone, immunotherapy) are still decisive in the individualised, complex treatment strategy of cancer patients, but complementary medicine and scientific naturopathic methods are also important, and no other disease form is more important for which a holistic, comprehensive approach and treatment is more important than for cancer.

The first surprise of the clinical experience was that the breast ablation contraindicated due to the patient's cardiac status was not performed and 5 months after the treatment a mammography-proven regression was observed, one year later the previously 30 mm lobulated malignant pattern was reduced to 14 mm, the metastatic conglomerate of the axillary lymph node also shrank significantly. The detectable lymph nodes were surrounded by a cortical border of 2-3 mm. The patient is currently well balanced, has been taking 2x5 ml of Flavint7 daily for one and a half years and her cardiac status is very good.

In another patient, decompensated cirrhosis was compensated. In our patient with inoperable gastric cancer who underwent exploratory laparotomy after Flavin7 intake, abdominal CT scan showed evidence of regression. Since September 2000, the patient's quality of life is good, he has gained 10 kg, he works and drives a car. We also have positive experience with other disease groups such as Alzheimer's disease, psoriasis, gravis arteriosclerosis, diabetes, viral infections. Additional human observations are currently carried out by nearly 100 general practitioners and 20 specialists.

"For preventive purposes, we respectfully recommend this product to the Director of the Public Health Programme Office." - Dr. Sándor Erdős

Source: *Erdős, Sándor; Szabó, László; The role of flavonoids in health maintenance and cancer treatment; KOMPLEMENTER MEDICINA 5 : 4 pp. 54-55., 2 p. (2001)*

2000

The writings of Dr Zsuzsa Kovács, whose research formed the basis for the creation and further development of Flavin7 products.

Analysis of non-volatile organic compounds in red wines from Eger

Dr. Zsuzsanna Kovács †
assistant professor
1964 - 2004

Abstract: Analytical testing of products intended for human consumption is currently of fundamental importance worldwide, particularly in the environmental and health context. In the recent past, in many countries it was almost impossible to sell wine without quality certification based on modern instrumental analytical methods. There is well-established biomedical evidence for the antioxidant and vascular wall-protective effects of wine in moderate consumption. On the other hand, wine consumption may also play a role in the prevention of heart attacks. The most important constituents of wine for these biological effects are flavonoids, anthocyanidins and their glycosides. Anthocyanins are mainly found in red wines. The organic components have a characteristic antioxidant activity which may play an important role in health protection. In our studies, volatile and non-volatile organic compounds were investigated in different wine varieties from Eger and Tokaj. We believe that this type of research project is of unique economic importance and is not negligible in a national context. The separation and determination of volatile compounds was carried out using the Finnigan GSQ GC-MS instrument, and non-volatile compounds were determined using HPLC-DAD and FAB MS techniques.

Source: *Zsuzsanna Kovács, Zoltán Dinya, Examination of non-volatile organic compounds in red wines made in Eger, Microchemical Journal - New York, Volume 67, Issues 1-3, 2000, Pages 57-62, ISSN 0026-265X,*

LC-SSI-MS techniques as efficient tools for the characterization of non-volatile phenolic compounds in a special Hungarian wine

Abstract: The utility of high-performance liquid chromatography-mass spectrometry using electrospray (ESI) and sonic spray (SSI) ionization for the characterization of non-volatile phenolic compounds was tested using a special Hungarian wine Tokaj aszú 1983. In addition to caffeic, ferrullic, chlorogenic and 3,4-dimethoxy cinnamic acid; 3,4-dimethoxy cinnamoyl, ferruloylic and galloyl glucose; gentisic acid p-D-glucoside; theogallin; and resveratrol 3-O-β-D-glucoside, 26 flavonoids were identified. It has been shown that SSI is a more effective tool for characterizing and monitoring non-volatile phenolic compounds than ESI due to its higher sensitivity.

Source: *Kovács Zs, Dinya Z, Antus S. LC-SSI-MS techniques as efficient tools for characterization of nonvolatile phenolic compounds of a special Hungarian wine. J Chromatogr Sci. 2004 Mar;42(3):125-9. doi: 10.1093/chromsci/42.3.125. PMID: 15023247.*

Statistical evaluation of the aroma and metal content of Tokaj wines

Abstract: The quality of wine is largely determined by the qualitative and quantitative composition of the organic and inorganic components present, and therefore their identification is one of the most important tasks of wine analysis. From an economic point of view, however, it is of unique importance to continuously check that the quality of the wine is satisfactory. In view of the trend towards products for human consumption, only those that are able to meet the quality requirements of a progressively increasing demand are likely to be successful on the market in the long term. Food analysis research, on the other hand, plays a very important role in the protection of origin, which is particularly important in a wine-growing area with such a long tradition. The study sought to answer the question of how the qualitative and quantitative relationships of volatile organic and metallic compounds present in the traditional wines produced in the production area depend on the vintage, the place of production and the type of grape and how these are specific to the type and vintage of wine. © 2000 Elsevier Science BV

Source: *Zoltán Murányi, Zsuzsanna Kovács, Statistical evalution of aroma and metal content in Tokay wines, Microchemical Journal - New York, Volume 67, Issues 1-3, 2000, Pages 91-96, ISSN 0026-265X,*

ABOUT STEM CELLS - OLIMPIQ STEMXCELL

The most important question in current stem cell research is how to increase the number of adult stem cells. If we can get our bodies to produce more stem cells naturally, the body itself will be able to correct defects that have arisen through disease, accident or simply ageing. The more stem cells in the bloodstream, the better our health. Bone marrow stem cells are the body's natural 'renewal' system. Stem cell levels are one of the best indicators of health. Better than cholesterol, blood pressure or blood sugar. The number of stem cells in 5 litres of blood varies between 5 million and 25 million. As we age, the number of stem cells produced decreases significantly. After the age of 35, people recover more slowly and with greater difficulty because stem cells are not produced at the same rate as when they are younger. Stem cells are non-specialised cells that can divide and regenerate indefinitely. After conception, the zygote that migrates through the fallopian tubes to the uterine cavity and then embeds in the cavity is still made up of totipotent (capable of anything) cells. The specialisation of these cells into nerve, brain, muscle, skin, etc. cells begins on day 15 of embryonic development. In these cells, different stages of genetic material (DNA) are activated and the development of the individual begins. The cost is that they lose their "totipotent" capacity. During embryonic development, however, some of these "totipotent" tissue cells are preserved. These are called tissue stem cells (haemopoietic) and are derived from the umbilical cord at birth.

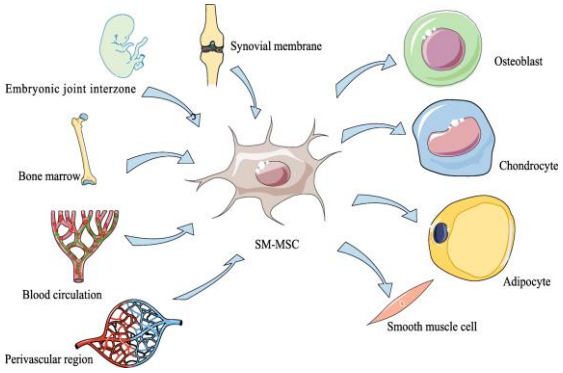


Figure 1: Possible differentiation of stem cells

The scientific world has long been aware that higher stem cell levels can lead to greater regeneration and tissue renewal. Our aim was to look for plant compounds that could help increase stem cell levels. Our research, which began in 2006, was successful and the study below is one of the first to show that it is possible to increase stem cell levels from bone marrow using plant compounds.

2012

**Plant compounds can affect stem cell levels.
Stem cells in the peripheral blood can contribute to tissue regeneration because they can form somatic cells. This allows tissues to regenerate, and organs that are not functioning properly can regain their original capacity.**

Plant compounds increased the level of CD34 positive cells in peripheral blood

Abstract: Peripheral blood stem cells can contribute to tissue regeneration by their ability to form somatic cells. Therefore, CD34+ stem cells or endothelial progenitor cells are considered biomarkers. According to the literature, natural substances can increase the release of CD34 positive (CD34+) cells. In this study, we investigated the baseline proportion of CD34+ cells in peripheral blood by flow cytometry. Mice were then treated with a newly developed herbal drug mixture and CD34+ stem cell levels were measured at 1, 3, 6, 18 and 24 hours after treatment.

The plant compounds used increased the number of CD34+ stem cells.

Although the stem cell count in peripheral blood varies individually and to a large extent, the fluctuation can be used as a biomarker for risk assessment, as with other peripheral blood compounds.

Original article : *Herbal compounds increased the level of CD34 positive cells in peripheral blood - An experimental work.Acta Alimentaria, Vol. 41 (1), pp. 19-25 (2012, DOI: 10.1556/AAlim.2011.0001*
Full text: http://medpublics.com/docs/OlimpiqSXC_Herbal_compounds.pdf

We know that the mobilisation of bone marrow stem cells and progenitor cells can be induced by different cytokines, growth factors, etc. This procedure is widely accepted in therapy, for example before bone marrow transplantation. In addition, there are marine algae that can increase stem cell levels within a short time (1 hour) after treatment, enhance regeneration or have a chemopreventive effect. These results suggest that there are nutrients that can promote regeneration. We call this natural regenerative medicine.

The leaders of the research
Prof. Dr. István Kiss and Prof. Dr. István Ember

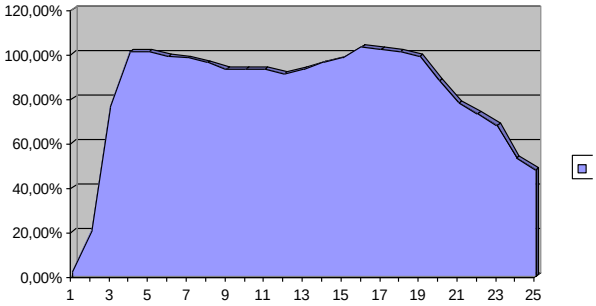


Figure 1: Stem cell level development after Olimpiq StemXCell

There were six female and six male mice in each group (6-8 weeks old). Their weight was 20 ± 4 g. For the experiments, peripheral blood samples (0.1 ml) were taken from the tail vein of the mice. The stem cell count of the blood samples was determined by flow cytometry. For the assay, algae, amino acids, polysaccharides and other plant components were used, i.e. the components of the Olimpiq StemXCell formulation.

The results of the study suggest that the agents used are able to mobilise bone marrow stem cells and consequently enhance haematopoietic regeneration after chemotherapy and make supportive therapies more successful.

Original article : *Herbal compounds increased the level of CD34 positive cells in peripheral blood - An experimental work.Acta Alimentaria, Vol. 41 (1), pp. 19-25 (2012, DOI: 10.1556/AAlim.2011.0001*
Full text: http://medpublics.com/docs/OlimpiqSXC_Herbal_compounds.pdf

2012

Stem cells may help treat diabetic retinopathy and nephropathy - recent research using the previous Wistar rat (+ Alloxan) model.

Stem cell stimulation-induced changes in retinal and renal vascular permeability in alloxan-induced diabetic rats as measured by fluorescein extravasation

Abstract: Our aim was to determine whether treatment with Olimpiq® StemXCell stem cell stimulator prevents the increase in retinal and renal vascular permeability in alloxan-induced diabetic rats. **MATERIALS AND METHODS:** Two groups of Wistar rats were induced diabetic by a single intraperitoneal injection of alloxan. The third, control group, received only laboratory chow. One diabetic group received Olimpiq® Stem×Cell treatment for 4 weeks. Blood-retinal barrier (BRB) and renal vascular permeability were measured by extravasation of bovine serum albumin labeled with fluorescein. **RESULTS:** Six weeks after Alloxan injection, significantly increased tissue fluorescence, renal vascular leakage and BRB degradation were detected in the diabetic group compared to the non-diabetic group. Olimpiq® Stem×Cell treatment significantly reduced BRB degradation, tissue fluorescence and vascular leakage.

Conclusion: Olimpiq® StemXCell may be a useful choice for the treatment of complications associated with increased vascular permeability in diabetes, such as retinopathy or nephropathy.

Diabetes is currently a major epidemiological problem worldwide due to the large number of people affected. Diabetes causes more than 1 million deaths per year, and nearly 80% of cases occur in low and middle income countries. Diabetes is the most common cause of retinopathy, which causes severe visual impairment and blindness. Several studies show that 15 years after the onset of diabetes, 2% of patients go blind and 10% suffer from severe visual impairment. 20-30% of people with diabetes suffer from nephropathy, which can lead to chronic kidney failure, eventually requiring dialysis. Diabetes is the most common cause of kidney failure in

adults worldwide in developed countries and causes death in 20% of cases.

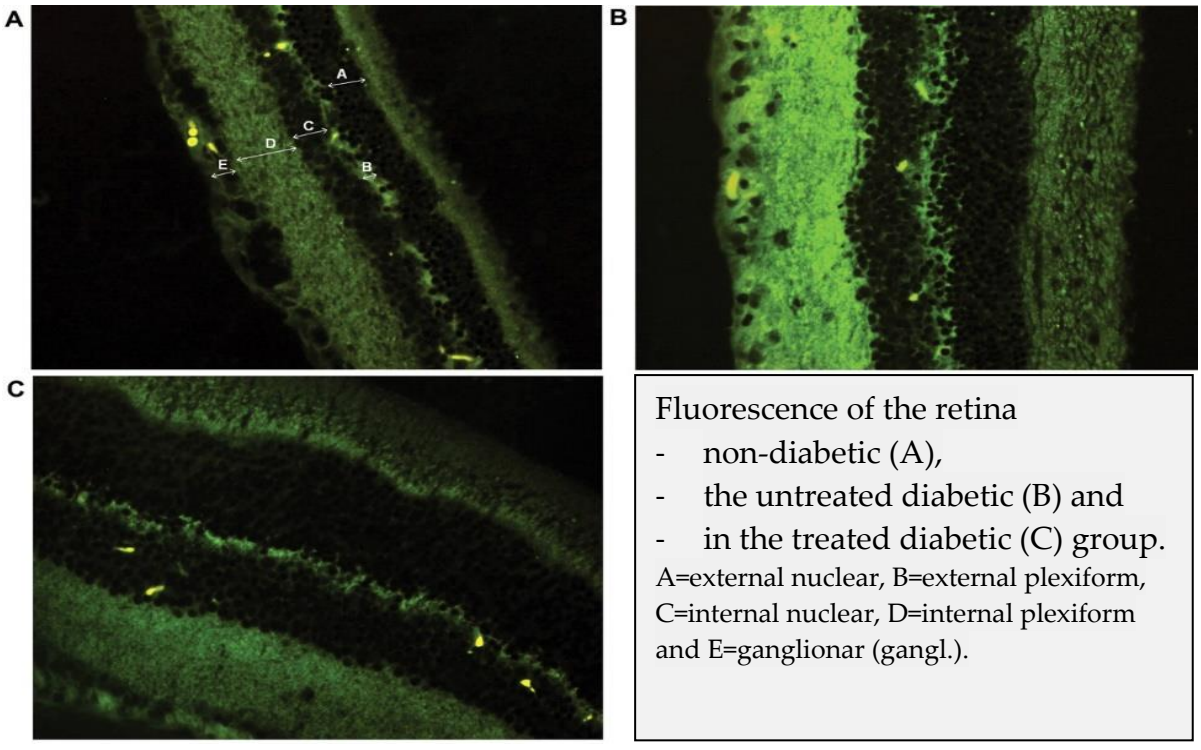
Preventing the spread of diabetes is particularly important to us, so in 2011-2012 we spent a lot of our research time and money on this. Two of the most well-known complications of diabetes are nephropathy and retinopathy. We were curious to see how the Olimpiq StemXCell SL stem cell stem cell propagation formula we developed would affect these diseases.
As in the previous study, the present study examined several organs, the retina and the kidney.

Test 1: The retina

"The aim of our study was to find new and more effective ways to treat complications of diabetes based on vascular lesions. The breakdown of the blood retinal barrier is the most common lesion in diabetic retinopathy and is responsible for macular oedema, the most common cause of visual impairment in diabetic patients. Degradation of the blood-retinal barrier is characteristic of the early stages of vascular dysfunction in both human and experimental diabetes."- Z. Doczi-Keresztesi

Two groups of male Wistar rats (250-300 g) were made diabetic by a single intraperitoneal injection of alloxan (125 mg/kg body weight).After 24 h, blood glucose levels were measured and the rats were considered diabetic (fasting blood glucose was above 13.7 mmol/l). One group of diabetic rats was treated with Olimpiq Stem×Cell SL® (7.14 mg/kg/day, mixed with standard laboratory diet) for 4 weeks.

RESULTS: Retinal fluorescence showed differences between the groups studied. The retina showed differences in the retinal images. The five retinal layers are shown from right to left. The difference in tissue fluorescence between the three groups can be clearly observed.



Fluorescence of the retina
- non-diabetic (A),
- the untreated diabetic (B) and
- in the treated diabetic (C) group.

A=external nuclear, B=external plexiform, C=internal nuclear, D=internal plexiform and E=ganglionar (gangl.).

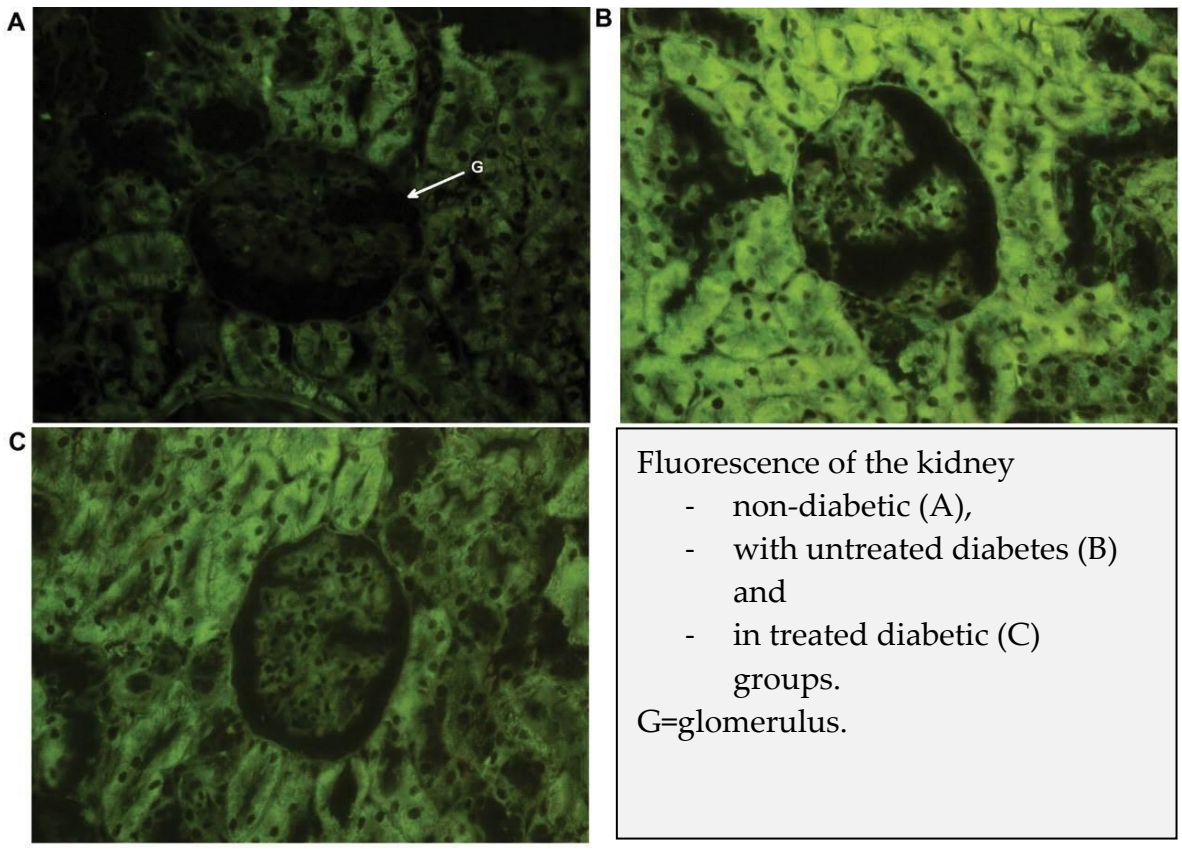
It appears that the mechanism of permeability reduction by stem cell stimulation, the structural repair of the vascular endothelium, has been achieved.

"Olimpiq® StemXCell SL would be a useful choice for the treatment of complications associated with increased vascular permeability in diabetes, such as retinopathy or nephropathy." - the authors

Test 2: The kidney

Diabetic nephropathy is a chronic impairment of kidney function in people with diabetes. Due to damage to the glomeruli, protein loss in the urine can become massive and cause low serum albumin levels, leading to generalised body swelling (oedema) and nephrotic syndrome. Similarly, the estimated glomerular filtration rate may gradually decrease from a normal value above 90 ml/min/1.73m^2 to below 15 ml/min and end-stage renal disease may be diagnosed. The pathophysiological abnormalities of diabetic nephropathy begin with long-standing, poorly controlled blood glucose levels. In our experiment, we used the model described above.

From the images documented as a result of the study, it is clear that the Olimpiq StemXCell SL® used is specifically designed to treat diabetes. Its active ingredients appear to play a role in improving the lives of diabetics and ensuring balanced blood glucose levels, as well as preventing complications and improving the body's ability to regenerate in both types of diabetes.



Fluorescence of the kidney
- non-diabetic (A),
- with untreated diabetes (B) and
- in treated diabetic (C) groups.

G=glomerulus.

Source: *Doczi-Keresztesi Z, Jung J, Kiss I, Mezei T, Szabo L, Ember I. Retinal and renal vascular permeability changes caused by stem cell stimulation in alloxan-induced diabetic rats, measured by extravasation of fluorescein. In Vivo. 2012 May-Jun;26(3):427-35. PMID: 22523295.*

2010

Bone marrow stem cells have been found to differentiate into many cell types, such as cardiac myocytes, neurons, liver cells, etc. Researchers have recently provided evidence that stem cells can be mobilised from the bone marrow by ingestion of natural substances and hypothesised that continued dietary stimulation of stem cell production may help in the prevention/treatment of degenerative diseases.

Enhancing organ regeneration in animal models with a stem cell stimulating plant mixture

Abstract: Adult stem cells play an important role in the regeneration of damaged organs. Attempts have been made to enhance stem cell production with cytokines to improve cardiac function after infarction. In the present study, we investigated whether dietary stimulation of stem cell production instead of cytokine injection accelerates organ regeneration in animals. Olimpiq StemXCell (Crystal Institute Ltd., Eger, Germany) is a dietary supplement containing plant extracts (previously shown to increase the number of circulating CD34+ cells). In the first experiment, carbon tetrachloride was used to induce liver injury in CBA/Ca mice and liver weights of StemXCell-fed and control animals were compared 10 days after treatment. In the second model, experimental diabetes was induced with alloxan in F344 rats.

Blood glucose levels were measured for 5 weeks in the control and StemXCell-fed groups. The third part of the study investigated the effect of StemXCell on cardiac function. Eight weeks after the isoproterenol compound induced myocardial infarction in Wistar rats, left ventricular ejection fraction was determined as a functional parameter of myocardial regeneration.

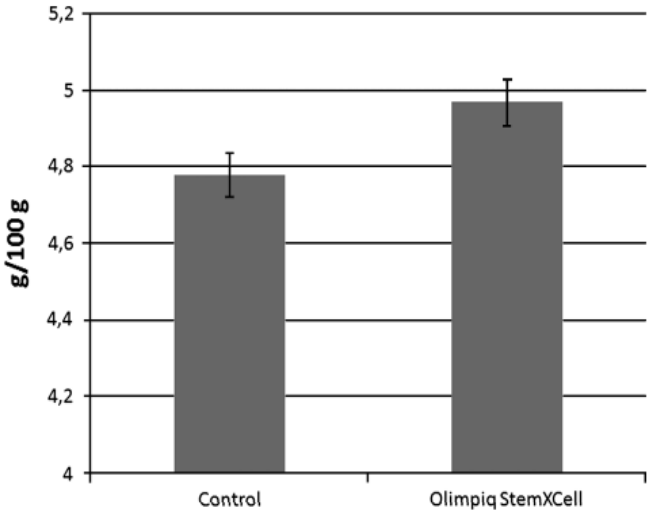
In all three animal models, StemXCell consumption statistically significantly improved organ regeneration *(relative liver weight: 4.78 +/- 0.06 g/100 g vs. 4.97 +/- 0.07 g/100 g; blood glucose at week 5, 16 +/- 1.30 mmol/L vs. 10.2 +/- 0.92 mmol/L, ejection fraction: 57.5 +/- 2.23 vs. 68.2 +/- 4.94; controls vs. treated animals).*
Our study supports the hypothesis that dietary enhancement of stem cell production may protect against organ damage and promote regeneration.

Source: *Kiss I, Tibold A, Halmosi R, Bartha E, Koltai K, Orsós Z, Bujdosó L, Ember I. Enhancement of organ regeneration in animal models by stem cell-stimulating plant mixtures. J Med Food. 2010 Jun;13(3):599-604. doi: 10.1089/jmf.2009.0013. full text: http://medpublics.com/docs/OlimpiqSXC_Enhancement.pdf*

Test 1: The liver

Liver problems can also be caused by a number of factors that damage the liver, such as viruses, alcohol consumption and obesity. Over time, conditions that damage the liver can lead to scarring (cirrhosis), which can lead to liver failure, a life-threatening condition. However, early treatment can give the liver time to heal. The differentiation of stem cells into hepatocytes has been extensively studied, both in vitro and in vivo. In all cases, studies on liver failure have demonstrated the protective effect of stem cell therapy.

In our previous experiments, we investigated the effect of a complex mixture (Olimpiq StemXCell, dietary supplement DOI: 10.1556/AAlim.2011.0001) on circulating stem cell concentration and found that it statistically significantly increased circulating CD34+ cell numbers. In the present study, we investigated whether this increased stem cell count is associated with any functional improvement in conditions associated with visceral injury. In the experiment, carbon tetrachloride was applied to CBA/Ca mice to induce liver injury, and the liver weights of StemXCell-fed and control animals were compared 10 days after treatment. The relative liver weights of experimental and control animals in the liver injury model are shown in the figure.



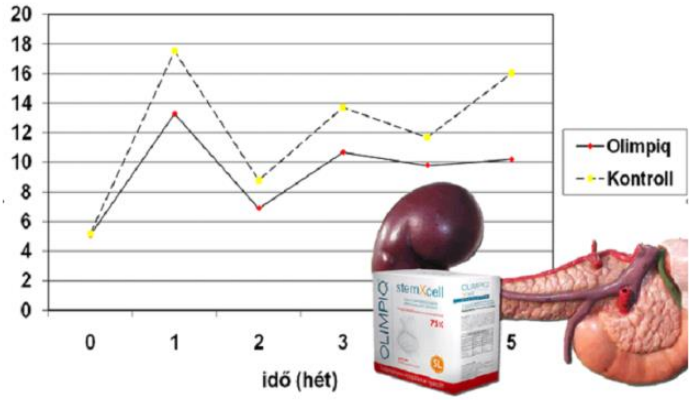
CBA=Relative liver weights of Ca mice (12 animals per group) after consumption of Olimpiq StemXCell. The results of the experiment showed that StemXCell treatment resulted in increased liver weight compared to the control. The difference was statistically significant (P=0.0462). The results indicated a faster liver regeneration (relative liver weight, 4.78 +/- 0.06 g=100 g vs. 4.97 +/- 0.07 g=100 g) after chemical liver injury.

Our results are in line with previous experiments and support our original hypothesis that dietary enhancement of adult stem cell production may increase the regenerative potential of several organs.

Test 2: The pancreas

To determine whether treatment with Olimpiq StemXCell stem cell enhancer could prevent hyperglycaemia-induced increases in retinal and renal permeability and inhibit blood-retinal barrier breakdown, we had to establish the conditions of alloxan-induced diabetes.

Three groups of male Whistar rats were used. Two of the groups were given a single intraperitoneal injection of alloxan (125 mg/kg) - a toxic substance that destroys insulin-producing beta cells in the pancreas, the third group received only laboratory feed. One group of alloxan-induced diabetic rats was treated with Olimiq StemXCell for 4 weeks. The blood-retinal barrier and renal artery permeability were measured by bovine serum albumin (FITC-BSA)-labelled fluorescein isothiocyanate leakage.



After six weeks of alloxan treatment, significant tissue fluorescence, renal leakage and blood-retinal barrier (BRB) degradation occurred in the diabetic group compared to the non-diabetic group.

Treatment with a stem cell enhancer significantly reduced BRB degradation, tissue fluorescence and vascular leakage compared to the untreated group. The mechanism of these effects may involve vascular regeneration induced by stem cell stimulation.

The results of the study suggest that Omlimpiq Stemxcell may be useful in the treatment of complications of diabetes, such as nephropathy and retinopathy, which are associated with increased vascular permeability. The graph shows the changing blood glucose levels, which is representative of the normalisation of blood glucose levels in the stem cell enhancing group.

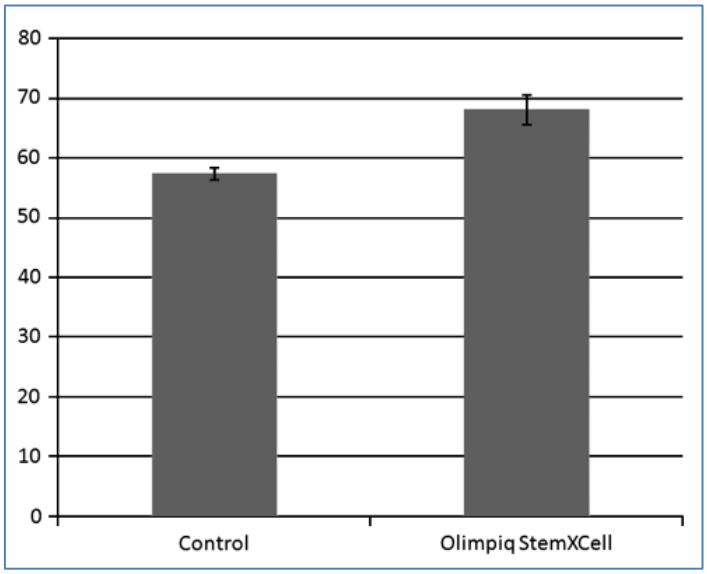
Test 3: The heart

What is the ejection fraction? The ejection fraction is a measure of how healthy the heart is. A low ejection fraction can indicate heart failure and can lead to a number of symptoms, including. Ejection fraction refers to the percentage of blood pumped out of the left ventricle with each heartbeat.

In the present study, we investigated whether dietary stimulation of stem cell production rather than cytokine injection accelerates organ regeneration in animals.

Cardiovascular studies have shown a positive effect of StemXCell treatment:
Ejection fraction as a parameter of cardiac function in Wistar rats (five rats in the control group and 10 animals in the StemXCell group), 8 weeks after Olimpiq StemXCell treatment.

In the experiment, the effect of StemXCell on cardiac function was investigated. Eight weeks after induction of myocardial infarction in rats with isoproterenol, left ventricular ejection fraction was determined as a functional parameter of myocardial regeneration. In animal models, StemXCell consumption improved cardiac regeneration (ejection fraction, 57.5 +/- 2.23 vs. 68.2 +/- 4.94; control vs. treated animals, respectively) in a statistically significant manner ($p=0.0383$). Our study confirms the hypothesis that dietary enhancement of stem cell production may protect against organ injury and promote regeneration.



"Our present study confirms the possibility that stem cell mobilisation or enhancement of stem cell production by dietary means is a realistic option for achieving health benefits. It also seems very reasonable, based on the results of our acute and sub-acute trials, that chronic, moderate stimulation of stem cell production may have similar effects and may also have preventive effects against many chronic degenerative diseases, in line with the experience of conventional herbal therapy. To prove this, in addition to our ongoing chronic trials, further large-scale studies in this area are needed" - Prof Dr István Kiss, Head of Research

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