A SUMMARY
of THE STUDIES
on the two patented extracts
KLAMIN® and APHAMAX®

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STUDIES on the KLAMIN® EXTRACT

Klamin®, neuronal stem cells and brain/nervous system repair

Sedriep S. et al., **Beneficial nutraceutical modulation of cerebral erythropoietin expression and oxidative stress: an experimental study,** J Biol Regul Homeost Agents. 2011 Apr-Jun;25(2):187-94.

In this study one group of "subnormal" **mice** (accelerated senescence) and one group of "normal" **mice**, were subjected to the Morris Test on learning ability, a test that uses an aquatic labyrinth which the mice must learn to exit. The "subnormal" mice employs on average **25 seconds** to get out; while the "normal" mice takes about **9 seconds**. After the administration of Klamin®, **the subnormal mice became normal, taking only 10 seconds** to get out; while **the "normal" mice became super, taking only 4 seconds** to get out! At the end of the study, the brain of the mice was analyzed, and a **strong increase in cerebral erythropoietin (EPO) in the brain** was found. Cerebral **EPO is the mother of all neuronal stem cells**, and through them **of all neurotransmitters**, giving the product the ability to contribute to the repairing of any damage to the brain and the nervous system.

Studies on EPO (Erythropoietin)

Klamin® is a source a bioavailable PEA (phenyethylamine), and we have seen how it stimulates endogenous brain erythropoietin. Let's look at some of the studies relative to EPO (erythropoietin).

Wang Y et al., **Hydrogel delivery of erythropoietin to the brain for endogenous stem cell stimulation after stroke injury**. Biomaterials. 2012 Mar;33(9):2681-92.

This study, performed at the University of Toronto, proposes a delivery of EPO in the brain, as a way of stimulating endogenous neural stem cells.

Zhi-Yong Chen, et al., **Endogenous Erythropoietin Signaling Is Required for Normal Neural Progenitor Cell Proliferation,** JBC Papers in Press, June 28, 2007,

This confirms that the **endogenous production of brain EPO**, which we have seen is significant stimulated by Klamin®, is **necessary for the normal metabolism and proliferation of neuronal stem cells.**

Borhani-Haghighi A. et al., **Erythropoietin for acute multiple sclerosis in patients with optic neuritis as a first demyelination event**. Neurosciences (Riyadh). 2012 Apr;17(2):151-5.

EPO is proposed as a **potential cure for Multiple Sclerosis** and to prevent demyelination, which is the first stage of MS.

Assaraf M.I. et al., **Brain erythropoietin receptor expression in Alzheimer disease and mild cognitive impairment**, J Neuropathol Exp Neurol. 2007 May; 66(5):389-98.

Lee ST et al., **Erythropoietin improves memory function with reducing endothelial dysfunction and amyloid-beta burden in Alzheimer's disease models**. J Neurochem. 2012 Jan;120(1):115-24.

In the two studies above, the role of EPO in **cognitive impairment**, up to senile dementia and **Alzheimer's**, is acknowledged, together with the ability to improve memory and reduce the beta-amyloid burden that is si prevalent in Alzheimer's.

Klamin®, ADHD & Autism

Cremonte M, Scoglio S et al.**, The effect of experimental supplementation with the Klamath Algae Extract Klamin® on Attention Deficit/Hyperactivity Disorder,** *Journal of Medicinal Food,* December 2017(in publication).

In this study, 30 children **diagnosed with ADHD** were administered Klamin®, at dosages variable from 250 mg to 1.2 grams (according to weight). At the end of the study, there were **significant improvements in the overall functioning of the child**, as well as in the psychiatric scales with which they were evaluated, such as: **levels of attention**; **levels of**

hyperactivity; **executive functions**; **quickness** and **precision** in the performing of tests such as the Bells test. The majority of the subjects continued using the product even after the free administration for the study ceased. The researchers also found significant improvements in the 25% of children who were also affected by **autism**.

Klamin® and MAO-B inhibition

Scoglio S. et al., **Selective MAO-B inhibition by an Aphanizomenon flos-aquae extract and by its constitutive active principle phycocyanins and mycosporine-like aminoacids**, Phytomedicine, 2014 Mar 29, pii:S0944-7113(14)00123-8.

Here we proved the ability of both AFA-phycocyanins and mycosporine-like amino acids (MMAs) to inhibit the monoaminoxidase-B enzymes (MAO-B), responsible for the breakdown both of PEA and monoamine neurotransmitters such as dopamine, thus both allowing PEA to work, and enhancing the dopaminergic cascade (leading both to higher energy and libido).

Klamin®, mood disorders and menopause

Genazzani A.D. et al., **Effects of Klamath Algae extract on psychological disorders and depression in menopausal women: a pilot study.** *Minerva Ginecol.* 2010 Oct;62(5):381-8. Italian.

Study by the Department of Gynaecology of the University Hospital of Modena, on 20 women (+ 20 for placebo control) during menopause and with psychosomatic symptoms associated with menopause. The intake of only 1 gr./die of the Klamin® extract resulted in **very significant improvement**, measured with specific psychiatric scales, i.e. **depression, anxiety and self-esteem**. Particularly relevant is the fact that the same extremely significant result was obtained in relation to both depression and anxiety, which are usually treated with different drugs. This fact confirms how Klamin® acts as a general neuromodulator.

Scoglio S, Benedetti S, Genazzani AD et al., **Effect of a 2-month treatment with Klamin, a Klamath algae extract, on the general well-being, antioxidant profile and oxidative status of postmenopausal women.** Gynecol Endocrinol. 2009 Apr;25(4):235-40.

This study evaluated certain gynaecological scales with good results regarding the various psychosomatic parameters (from hot flushes to depression). Evaluation of the lipoperoxidation status of patients was performed: there was a significant **reduction (approximately 35%) of the MDA,** the main marker of lipo- peroxidation, one of the main causes of degenerative diseases); further, there was an **increase, between 30% and 42%, of the main anti-oxidant nutrients,** such as beta, alpha and gamma carotenes, lutein and zeaxhantin, alpha and gamma tocopherols and of plasma retinol (+16%).

Akinobu Tsunoo, M.D., **Klamin®, an algae derived supplement, for depression.** Published in Japan.

In this study carried out by a Japanese medical team, and published in Japanese, 16 moderately depressed patients took 1 gr. of Klamin® for 60 days, while 5 patients took a placebo for the same period. While for the latter group their clinical picture worsened, the 16 patients taking Klamin® had a substantial improvement in their depression without any side-effects on the hepatic and renal functions, and without alteration of the thyroid metabolism.

Study on depression – Department of Psychiatry, Hospital San Raffaele, Milan (unpublished).

16 patients with moderate depression, who did not want or did not respond in a positive manner to pharmaceutical treatments, added a small quantity (about 500 mg.) of Klamin for one month. **Despite the small quantity and the reduced period, half of the patients reported a significant improvement of their condition**.

Bellingeri P., Scoglio S., **Complementary treatment of mood disorders associated with oncological diseases by using the Klamath algae extract Klamin® : a pilot study** (in preparation for publication).

In this study, by the Ovada Oncology Center (Italy), 18 **terminally ill cancer patients**, being treated only with palliative care, took approximately 1 gr. of the

Klamin® extract for 2 months. Their condition was evaluated with specific VAS scales (from 0 to 10) on **Anxiety, Fatigue and Depression**. **Statistically significant improvements in all three areas were observed**, confirming that Klamin® is able to balance even apparently conflicting states such as anxiety and depression and to sustain the capacities of the body to produce energy. This is a particularly valuable study, given the extreme condition that was treated.

Klamin®, digestion and metabolic syndrome

Kushak, R., et al., **Effect of Algae Aphanizomenon Flos Aquae on Digestive Enzyme Activity and Polyunsaturated Fatty Acids Level in Blood Plasma**. *Gastroenterology*, 1999, 116:A559.

A study performed on mice, which has shown that Klamath algae may contribute to the **normalization of glycemic metabolism** thanks to its ability to partially inhibit the action of certain enzymes (**alpha-amylase, sucrase and maltase**) responsible for the absorption of sugars. Given that most of enzyme inhibition activity is performed by phycocyanins and MAAs, it is very plausible to expect that the same activity, beneficial for the so-called metabolic syndrome, is performed by both Klamin® and Aphamax®, the former having a high concentration of MAAs, the latter of AFA-phycocyanins.

Ohta H. et al., **Tyramine and β-phenylethylamine, from fermented food products, as agonists for the human trace amine-associated receptor 1 (hTAAR1) in the stomach**, *Bioscience, Biotechnology, and Biochemistry*, DOI: 10.1080/09168451.2016.1274640

Many organs have receptors for PEA, including **the stomach**: the pylorus is especially rich in TAAR1 (the specific receptor for PEA), and when PEA attaches to the receptor, gastrin is produced, which stimulates **gastric secretions**, thus leading to **a better digestive activity**. This means that Klamin® can also improve digestion.

Klamin® and the immune system

Jensen G.S. et al., **Consumption of Aphanizomenon flos-aquae has rapid effects on the circulation and function of immune cells in humans.** Journal of the American Nutraceutical Association, 2000 (2): 50–58.

The intake of 1.5 gr. of Klamath algae in human subjects generates an overall activation of the immune system, and of its main cells: **macrophages**, PMN cells T and B, and most of all **NK cells**, which are not just strengthens but also mobilized. In fact, within one month of taking the algae, about 40% of NK cells are pushed from the blood into organ and tissues for 4-6 hours after intake. This is extremely important, because the most known immune activating substances, such as Echinacea, also promote the strengthening of NK cells, but not their mobilization (it is as if an army were distributed better weapons, but then they remain inside their barracks). Klamath algae also modulates the activity of the PMN (polymorphonucleated) cells, making them more effective and precise, and thus also reducing the inflammation derived from the free radicals production of these important components of our immune system. **Recent studies have proven that it is in fact PEA that is responsible for such general activation and mobilization.**

Babusyte A. et al., **Biogenic amines activate blood leukocytes via trace amine-associated receptors TAAR1 and TAAR2**, *Journal of Leukocyte Biology,* 93: 387–394; 2013.

Nelson D.A. et al., **Expression of Neuronal Trace Amine-associated Receptor (Taar) mRNAs in Leukocytes**, J Neuroimmunol. 2007 Dec; 192(1-2): 21–30.

These two studies above establish the role of **PEA as a general modulator of the immune system**, able to activate and mobilize T and B cells, macrophages, NK cells, the elite force of our immune army. This explains why people who take Klamin® tend to be relatively immune for the winter illnesses (and the winter's blues). This also proves that, while when taking the whole algae one should take 1.5 grams 3 times a day, every 4-6 hours, with Klamin® (and Klamax®) it is enough to take 1/2 dose 3 times a day (or dissolve 1.5 doses in a bottle of water, and drink it during the day) to have the same immune-enhancing effect.

Klamin® and pain

Mosnaim AD et al., **Analgesic effects of β-phenylethylamine and various methylated derivatives in mice**, *Neurochem Res*. 2014 Sep;39(9):1675-80.

This study confirms an effect that I have witnessed myself many times with Klamin®, the main ingredient of Klamax®: the analgesic effect of PEA, its ability **to reduce or eliminate pain r**elatively quickly. This is also why liquid Klamin®, or Klamax® kept in the mouth for a minute or so, **can also help with migraines and headaches**, among other things.

STUDIES on the APHAMAX® EXTRACT

This section describes the studies regarding the anti-oxidant / anti-inflammatory / anti-proliferative and somatic stem cells activating properties of the specific AFA-phycocyanins present in Klamath algae, concentrated in the AphaMax® extract.

AFA-Phycocyanins anti-proliferative

Scoglio S. et al, **Inhibitory effects of Aphanizomenon flos- aquae constituents on human UDP-glucose dehydrogenase activity, in** *Journal of Enzyme Inhibition and Medicinal Chemistry,* 2016 Feb. 23.

This article proved the ability of the AphaMax® extract to significantly **inhibit the enzyme UDP-glucose dehydrogenase**, which is directly involved in the development of **cancer metastases**, thus adding a further important aspect to the general anti-cancer activity of this Klamath algae extract. Compared to other substances such as quercetine and gallic acid, while these compounds inhibited 64% the former and 73% the latter at a concentration of 500 micromolars, AFA-PC inhibited metastatic cells more than 90% at only 100 nanomolars, that is at a concentration of approximately 5.000 times lower!

Scoglio S. et al., **Study on the anti-proliferative effect of the AFA-PC on leukaemic cells Jukart in culture** - University of Urbino / Nutritherapy Research Center (in preparation for publication)

In this study at the University of Urbino, a standard model was used (the same model used for the Bechelli study reported above): a minimal dose of an extract of AFA-PC (10 micromoles) **inhibited the proliferation of leukemic cells in culture by almost 100%**; the datum is even more significant in light of the fact that similar studies, carried out with an extract of phycocyanins from Spirulina, obtained the maximum inhibition of 49% with a dose that was five times higher (50 micromoles).

AFA-Phycocyanins antioxidant

Benedetti S, Scoglio S, et al., **Oxygen radical absorbance capacity of phycocyanin and phycocyanobilin from the food supplement Aphanizomenon flos-aquae,** J Med Food. 2010 Feb;13(1):223-7.

This study, carried out at the University of Urbino, tested the anti-oxidant capacity of AFA-phycocyanins, the specific anti-oxidant and anti-inflammatory molecules of Klamath algae, through the known **ORAC test,** the standard official method to measure the anti-oxidant power of purified molecules. The result is that the anti-oxidant power of **AFA-phycocyanins is 40 times higher than the molecules considered as the most powerful anti-oxidant until now,** i.e. **catechins of green tea, and quercetin,** present in different vegetable substances**.**

Kuriakose GC, Kurup MG., **Evaluation of renoprotective effect of Aphanizomenon flos-aquae on cisplatin-induced renal dysfunction in rats.** Ren Fail. 2008;30(7):717-25.

This study, carried out by a team of Indian researchers, tested the capacity of an extract of AFA-phycocyanins from Klamath algae to **reduce kidney damage caused by cisplatin chemotherapy** Guinea pigs, obtaining extremely positive results: at a dosage of 100 mg. in mice subjected to chemotherapy, the extract gave as result nearly complete normality of the physiological values that had been significantly altered by the administration of cisplatin, one of the most toxic chemotherapic substances, in particular for kidneys. The normalized values are: creatinine; BUN (blood values of nitrogen), urea and MDA, the most significant marker of lipo-peroxidation, the destructive oxidation of the lipidic components of the cell membranes.

Kuriakose GC, Kurup MG, **Antioxidant and hepatoprotective activity of Aphanizomenon flos-aquae Linn against paracetamol intoxication in rats.** Indian J Exp Biol. 2010 Nov;48(11):1123-30.

The same Indian researchers tested the capacity of an extract of phycocyanins from AFA to inhibit the liver damage caused by paracetamol, suggesting AFA algae as a strong hepato-protector (confirming this property, demonstrated through decades of empirical cases).

Benedetti S., Scoglio S., et al. **Antioxidant properties of a novel phycocyanin extract from the blue-green alga Aphanizomenon flos-aquae**. Life Sci. 2004 Sep 24;75(19):2353-62.

A preliminary study, carried out by our research team of the Nutritherapy Research Center, tested the anti-lipoperoxidation properties of an extract of AFA- phycocyanins, producing particularly significant results, obtaining a 90% inhibition in the production of MDA (a marker of the oxidation of the cell's lipid membrane) with just 1/200th of the dose at which phycocyanins from Spirulina obtained the same degree of inhibition.

AFA-Phycocyanins anti-inflammatory

Cavalchini A., Scoglio S., **Complementary Treatment of Psoriasis with an AFA-phycocyanins product: a preliminary 10-cases study**, in International Medical Journal, Vol. 16, 3, pp. 221-4, Sept. 2009.

Dr. Cavalchini, a dermatologist at the San Martino Hospital of Genoa, Italy, tested an AphaMax® based product on 10 cases of various types of chronic psoriasis, which did not respond to pharmaceutical therapies, including the new "biological" drugs. By administering 3 tablets per day (equivalent to 3 “Dermax” capsules), **within 3 months 8 cases out of the 10 were cured**; during the following 3 months the ninth case was also resolved and the tenth subject showed significant improvements.

Canestrari F. et al, **Proprietà antinfiammatorie della ficocianina da estratto algale di Aphanizomenon flos aquae**, Progress in Nutrition, Vol. 8, n.2 (2006), pp. 99-103.

In this study, done at the University of Ferrara, the anti-inflammatory action of an extract of AFA-phycocyanins was tested. A group of mice were injected with capsaicin, the active principle of chili pepper, directly into the stomach, and a significant increase in inflammation was observed (through the Evans Blue marker measurement); in a second group of mice the injection of capsaicin was preceded by the administration of the AphaMax (AFA-phycocyanins) extract: in this second group **inflammation was almost completely inhibited, approximately 95%**! An even better result was obtained when

the same test was repeated injecting capsaicin on the urinary tract of the mice, with **a more than 100% inhibition**! The latter also shows that AFA-phycocyanins are very effective even after having gone through the G.I tract, and having been metabolized through our blood torrent.

Mondavio M., Scoglio S, **Study on fibromyalgia** (in preparation for publication)

In this study carried out by Dr. Mondavio, 20 female patients with fibromyalgia took 2 tablets a day of a product based on the AphaMax® extract for 2 months. At the end, **a significant reduction of the number of painful points** (acupressure test), as well as a significant reduction in articular stiffness and fatigue, occurred in 2/3 of patients.

AFA -Phycocyanins and somatic stem cells

Phycocyanins have been found to stimulate the release of fibroblasts, the most important of the somatic stem cells. More specifically, the studies have been done on the C-phycocyanins (C-PC) component extracted from Spirulina, but the study applies also to AFA-phycocyanins as they are also formed by C-PC. If anything the action of AFA-phycocyanins is superior, as it has been proven every time the two types of phycocyanins have been compared.

Madhyastha H.K. et al., **Purification of c-phycocyanin from Spirulina fusiformis and its effect on the induction of urokinase-type plasminogen activator from calf pulmonary endothelial cells,** *Phytomedicine* 13 (2006), 564–569.

Madhyastha H.K. et al., **C-phycocyanin transcriptionally regulates uPA mRNA through cAMP mediated PKA pathway in human fibroblast WI-38 cells,** *Biochimica et Biophysica Acta,* 1760 (2006) 1624–1630.

These two studies proved the ability of C-phycocyanins, the phycocyanins sub-molecules present in all cyanobacterial algae (including Klamath, whose phycocyans we have seen are more powerful), to stimulate the mobilization of fibroblasts, the somatic stem cells that are dirty involved in the regeneration of the derma and the skin, acting thus also as powerful wound healing agents.