01
17

daacro

SPRING 2017

NEWS

Weleda // 10 years of health claims // Biomarkers in saliva: Melatonin // High level
EU research // Sport studies // NIS – Non-interventional studies // Premenstrual syndrome //
Short reports: daacro goes to China ++ Networks ++ Memberships

Dear reader,

It's that time again: We are happy to send you the latest issue of daacro's newsletter. Once again, we have compiled information and news from the varying fields of our research for you. While selecting topics, we focused on content that we think could be relevant to you and your product development, based on our conversations with you.

However, 10 years of health claims regulations and 10 years of daacro studies for health claims also provides an opportunity to pause and take stock. We started our operation with clinical studies and nutritional supplements as well as our psychobiological stress expertise. Next came clinical trials on pharmaceuticals (including Phase I) and studies on cosmetics, while experts such as sports scientists joined our team, further strengthening our expertise. Today we conduct clinical studies with healthy volunteers as well as specific patient groups in cooperation with clinics pertaining to a broad range of indications. For this purpose, we make use of our clinical site in Trier as well as select partners' sites at other locations. All of our studies have one thing in common: Our meticulous scientific procedure and quality standards at the highest level.

Contact us, our team is happy to take on your questions!

With best regards,

Dr. Juliane Hellhammer, PhD
Daacro founder and CEO

OUR TOPICS:

SAVE THE DATE

IN COSMETICS
APRIL 04-06, 2017
LONDON, UK

WORLD CONGRESS INTEGRATIVE MEDICINE & HEALTH
MAY 03-05, 2017
BERLIN, GERMANY

VITAFOODS
MAY 09-11, 2017
GENEVA, SWITZERLAND

CINP THEMATIC MEETING
JULY 20-22, 2017
PRAGUE, CZECH REPUBLIC

47TH ANNUAL MEETING ISPNE
SEPT. 07-09, 2017
ZURICH, SWITZERLAND

SUPPLY SIDE WEST
SEPT. 25-29, 2017
LAS VEGAS, NV, USA

FOOD MATTERS LIVE
NOV. 21-23, 2017
LONDON, UK

1 SUCCESSFUL TRIAL: A NUTRITIONAL SUPPLEMENT ALLEVIATES SYMPTOMS OF PREMENSTRUAL SYNDROME

A controlled clinical trial successfully tested a nutritional supplement with regard to its capacity to alleviate symptoms of premenstrual syndrome.

Forty women with a PMS diagnosis were investigated over a time period of four menstrual cycles. One observation cycle was followed by three cycles during which either the test product or a control product without active ingredients (placebo) was ingested. The women filled out an online symptom diary daily for the assessment of PMS impairment severity. Furthermore, symptom severity was assessed via the biomarkers cortisol, estradiol, progesterone and corticosteroid-binding globulin (CBG), which are closely associated with PMS. The study demonstrated that intake of the nutritional supplement lead to a marked improvement of premenstrual symptoms. The test product dominated successfully over the placebo and considerably improved state of health.

Further details will soon be available in a publication: The authors Katja Schmidt, Nicole Weber, Meir Steiner, Nadin Meyer, Anne Dubberke, David Rutenberg and Juliane Hellhammer are currently concluding the submision process and are happy to inform you when the article has been published.

2 10 YEARS OF HEALTH CLAIMS REGULATIONS IN THE EU

AND 10 YEARS OF DAACRO SUBSTANTIATING HEALTH CLAIMS

Since July 1st, 2007, health-related claims in advertisements or on the packaging of food products generally fall under the "principle of prohibition with the reservation of permission" unless they fulfill the general and specific regulation requirements, are permitted by the regulations and have been admitted to the list of permitted claims according to articles 13 and 14 of the regulations. This procedure is based on the so-called Health Claims Regulation 1924/2006, which were issued by the European Parliament and the Council of the European Commission on the above date and later amended.

Since then, claims regarding nutritional values or health effects must not only follow strict criteria, but also be based on convincing scientific evidence. Only when no doubt regarding the correctness of the nutritional value claim or effectiveness of the advertised substance remains, does the European Food Safety Authority (EFSA) grant its permission.

On the one hand, this means safety for the consumer, on the other hand, food manufacturers are often confronted with the challenge of investing their scarce resources usefully in order to obtain evidence-based statements about their products.

Here, our experience and scientific expertise in the field of clinical studies is highly valuable to our clients and cooperation partners. We provide consultation to the best of our scientific and regulatory knowledge when planning a clinical study, which is then conducted according to these high standards, allowing us to establish a solid database that also convinces the regulatory authorities.

3 SALIVA LAB TRIER: MELATONIN – MORE THAN JUST A SLEEP HORMONE

Synthesis of the neurohormone melatonin is extremely important for healthy sleep as it helps regulate the circadian rhythm. Melatonin production is inhibited by light and facilitated by darkness. About 2 hours before usual bedtime, the epiphysis begins secreting melatonin. Values rise until maximum hormone concentration is reached between 2:00 and 4:00 am and then sink back to low daytime levels. If melatonin secretion is inhibited, disorders of the circadian rhythm and therefore difficulties falling asleep as well as maintaining sleep may develop, followed by fatigue and irritability. As aging occurs, melatonin concentrations sink naturally. However, caffeine and artificial light (especially from screens) also inhibit melatonin release. Lack of sleep doesn't only influence the affected persons' quality of life and ability to perform, but can also result in health-related issues. Besides high blood pressure and chronic headaches, the immune system can also become weakened as melatonin is an important helper, defending against free radicals and regulating the activity and expression of certain antioxidants.

A saliva analysis provides quick and easy clarity pertaining to the body's own melatonin concentration, allowing appropriate therapeutic steps to be taken should a hormone deficiency or circadian shift be determined.

Melatonin and DLMO: The initiation of melatonin production is termed "dim light melatonin onset (DLMO)" and describes the point in time, at which circulating melatonin rises above a certain threshold level, in comparison to low daytime levels (Figure 1). The identification of DLMO is considered the gold standard to determine melatonin concentration and discover disturbances of the circadian rhythm. Sample collection begins 3 to 4 hours before usual bedtime (which should be determined using a diary), is comprised of several saliva samples collected in 30 or 60 minute intervals and is concluded 2 hours after usual bedtime (Figure 3). Using DLMO, sleep phase disorders (advanced or delayed phase, Figure 2) can be easily identified, so that the optimal time for the application of therapeutic approaches can be determined.

The following figures were provided by Salimetrics, USA. If you are interested in further information or scientific literature, please contact our lab management.

Figure 1

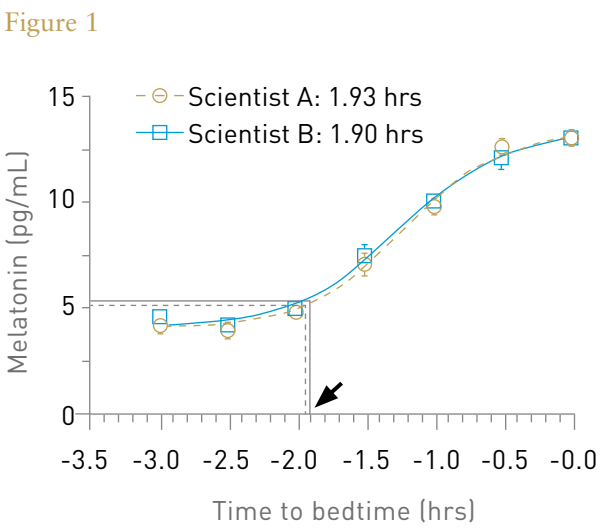


Figure 2

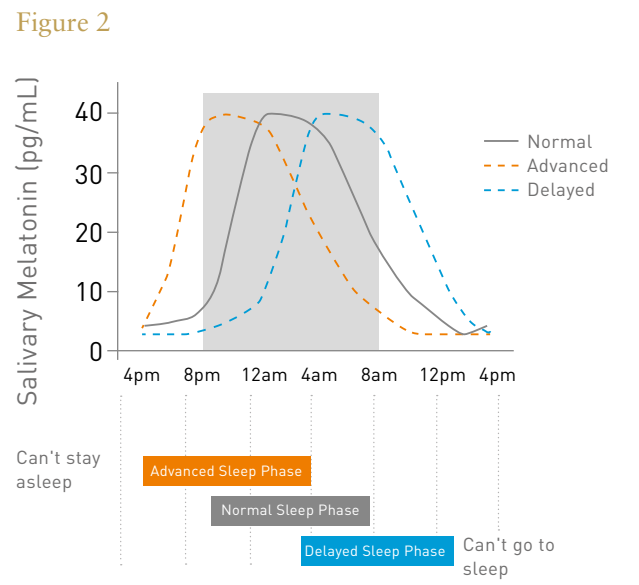


Figure 3

Normal bedtime

Time	7pm	8pm	9pm	10pm	11pm
Habitual Sleep Time (HRS)	-4	-3	-2	-1	0
Samples		1 2	3 4	5 6	7

4 SCIENTIFIC EXPERTISE – ESSENTIAL FOR SUCCESSFUL CLINICAL TRIALS

EU PROJECTS AND THEIR IMPORTANCE FOR CONTRACT RESEARCH

The European Food Safety Authority (EFSA) only allows health-related claims in advertisements or on the packaging of food products if these are convincingly evidenced by scientific studies. The EFSA's quality requirements for such studies are therefore very high. Alongside excellent regulatory knowledge, scientific expertise is thus of central importance in clinical studies.

The scientific aspects of study planning thereby include:

- A thorough review of the scientific literature to establish the current state of knowledge on the active ingredient and presumed mode of action
- Knowledge of and experience with well established methods as well as new and innovative methods suitable to demonstrate effectiveness
- Profound statistical understanding to interpret publications and plan clinical studies

Errors in these areas can have a serious impact on study results, completely distorting results in the worst case.

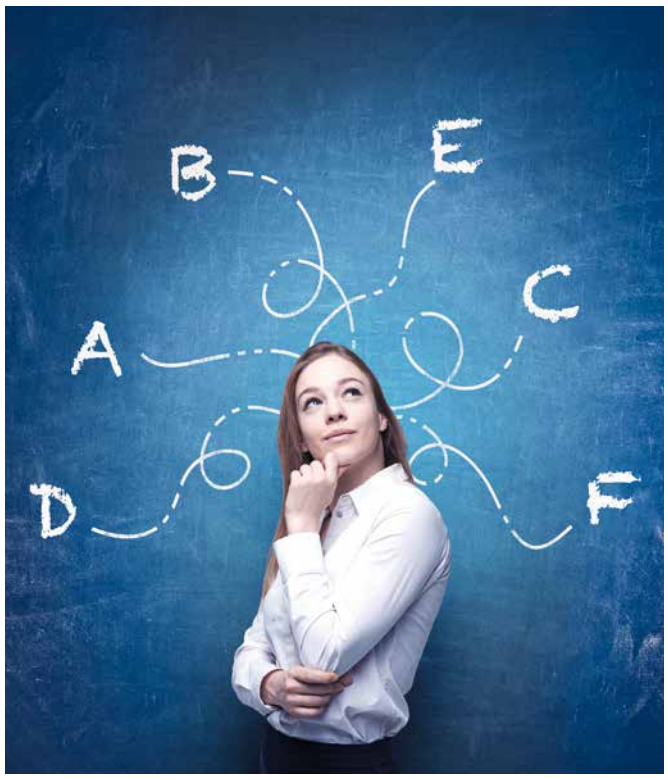
A research institute cannot employ experts from all clinical fields itself. Therefore it is of elementary importance to cooperate intensively with a network of internationally recognized experts. At daacro, this is made possible by our scientific advisory board on the one hand and our participation in scientific projects funded by the European Union on the other hand.

daacro has been a partner in the FP7-funded research project "Neurobiology and Treatment of Adolescent Female Conduct Disorder: The Central Role of Emotion Processing" since 2013. This international research project is investigating conduct disorders (CD) in children and youth (Project coordinator: Christine M. Freitag, MD, professor at Goethe-University Frankfurt/Main, Germany) from diverse perspectives. The project's aim is to expand knowledge on CD, especially in girls, and enable improved therapy. The consortium is comprised of 17 European partners (including 13 universities) from 8 countries. Daacro's saliva lab is participating in this research project, providing consultation, the organization of sampling materials, sample analysis, data transfer and biostatistical support.

In 2016, daacro received an additional research grant: Alongside two French firms Bionov (Robertet Group) and V@si, daacro is part of the Eurostars project **ActiveNutraLife***, which is developing a product that aims to accelerate the healing process of leukemia patients after chemotherapy. This new approach combines nutritional supplements, an online activity programme and novel stress diagnostics to measure individual exhaustion (cancer fatigue). Such ActiveNutraLife* kits are later to be distributed by health insurance providers. Within this project, daacro will develop a new variation of the stress diagnostics system neuropattern™. neuropattern™ is a procedure which enables an individualized diagnosis of stress-related disorders based on psychological, biological and symptomatic information. Results can be differentiated into 13 stress-related endophenotypes, the so-called "neuropatterns". The version adapted for leukemia patients, called HEMO-neuropattern, will concentrate on endophenotypes of exhaustion.

These two highly diverse research projects well document the daacro team's scientific recognition and reintroduce expert panels' current state of knowledge into our work.

*ActiveNutraLife – A new complementary medicine approach for the management of chemotherapy side effects



5 KNOW YOUR OPTIONS WHEN SELECTING A STUDY DESIGN

STUDY TYPE NIS: NON-INTERVENTIONAL STUDIES

In scientific research, we principally differentiate between primary and secondary research. While secondary research summarizes study results that are already available by conducting meta-analyses or reviews, in primary research, the actual studies are conducted. A further useful classification of study types in clinical and epidemiological research is interventional and non-interventional (NIS) or observation studies.

Study design selection and thereby study type dictates the study's quality, validity and worthiness of publication. Study type is determined by the research question and is the deciding factor regarding the scientific study's usefulness and interpretability.

Clinical trials are scientific studies that largely reduce influencing and confounding factors by employing inclusion and exclusion criteria as well as a precisely defined study protocol and treatment scheme. In contrast, non-interventional clinical studies are patient-focused observation studies in which patients are treated with an individually assigned therapy. NIS usually investigate pharmaceuticals that have already been licensed and follow an observation plan, which defines the observed case number, analyses methods and observation questions. No treatment specifications are made; the physician determines therapy based solely on medical diagnoses and patients are treated under normal practice conditions. Therefore, the aim of NIS is to observe and assess as large a number of patients as possible using a certain pharmaceutical. Evaluation is usually conducted retrospectively.

Therapy studies (non-interventional), prognosis studies, pharmaceutical observation studies, secondary data analyses, case series and case-by-case analyses belong to the group of NIS.

FROM THE DAACRO TEAM

Katja Schmidt

Statistics pro

Master's degree in applied mathematics (biomathematics profile, biostatistics specialization) from the Koblenz University of Applied Sciences - RheinAhr Campus. After her master's thesis, she started at daacro as a biostatistician.

Anne Dubberke

Lab team manager

Master's degree in biology (molecular genetics specialization) from Johannes Gutenberg University in Mainz were followed by work at the Institute of Epigenetics, Saarland University. Today she manages daacro's in-house saliva lab.

Melanie Eckelt

Sports pro

Sports sciences studies in Gießen (B.Sc., exercise and health specialization) and Karlsruhe (M.Sc., exercise and technology specialization). In 2016 she took over responsibility as data manager and for the field of sports studies.

6 WE CAN DO MORE THAN STRESS: SPORT STUDIES

NUTRITIONAL SUPPLEMENTS – INCREASED PERFORMANCE?

Nutritional supplements are concentrated sources of nutrients with physiological effects that augment normal nutrition. In the form of pills, tablets, capsules or fluids, a specific dose of nutrients can be supplied to the body. Nutritional supplements are used to compensate for nutrition-specific deficiencies or ensure the appropriate absorption of certain nutrients.

Professional athletes in particular, as well as amateur and recreational athletes, are increasingly relying on nutritional supplements to support muscle growth or fat loss, accelerate regeneration, compensate for an unbalanced diet or achieve a general performance increase. Athletes most commonly consume additional vitamins, minerals and amino acids in the form of nutritional supplements. The various effects of specific nutrients on the body have been investigated repeatedly and are therefore well known. However, individual circumstance, the exact composition of the nutritional supplement as well as the substance's stability all play an important role and must therefore be taken into account.

To test a product's exact effects, it is necessary to conduct a clinical study that is well thought through. Depending on the research question, various study designs and sports science test methods as well as established methods of performance diagnostics may be applied. Alongside questionnaires, these may include bioelectric impedance analyses, submaximal stress tests or strength measurements. We are happy to advise you with our longstanding expertise and our sports science know-how.

DAACRO GOES CHINA

Herbs and herbal mixtures are firmly established in traditional Chinese medicine ++ German quality standards desired ++ Consumption of vitamins and nutritional supplements are growing in China ++ Rhineland-Palatinate's ministry of economy and InnoNet HealthEconomy,a state health network, send a delegation to China ++ Stress expertise from daacro involved ++

DAACRO INVOLVEMENT IN PHARMA INDUSTRY

Member of DGPharMed and activity in the field of clinical trials ++

FRESH OFF THE PRESS

Olbrich, D. & Näher*, K. Changes to the cortisol awakening reaction (CAR) following stimulation with frequency-modulated music (AVWF®) – results from psychosomatic rehabilitation. Ärztliche Psychotherapie 2017; 12: 43–49.

*married and now Katja Schmidt, Biostatistician at daacro

PUBLICATION DETAILS

Publisher: daacro GmbH & Co. KG, Max-Planck-Straße 22, D-54296 Trier, Tel.: +49 (0)651 9120 494, info@daacro.de, www.daacro.de

Drafting and editorial staff: Dubberke, Eckelt, Hellhammer, Schmidt, Weber (daacro), Eitz (propeller)

Design: propeller, www.propeller.de

Photo credits: iStock Photo

Graphics: daacro, Salimetrics

7 WELEDA PRESENTS DAACRO STATISTICS ON NEURODORON®

RESULTS OF A POST-HOC ANALYSIS WERE PRESENTED AT THE EUROPEAN CONGRESS FOR INTEGRATIVE MEDICINE 2016 IN BUDAPEST: A CLINICAL TRIAL WITH NEURODORON® IN PATIENTS WITH NERVOUS EXHAUSTION.

In September 2016, Rebecca Hufnagel, clinical research – medical field at Weleda AG, presented a clinical study sponsored by the company and conducted by emovis GmbH, Berlin. We performed a post-hoc analysis with the data:

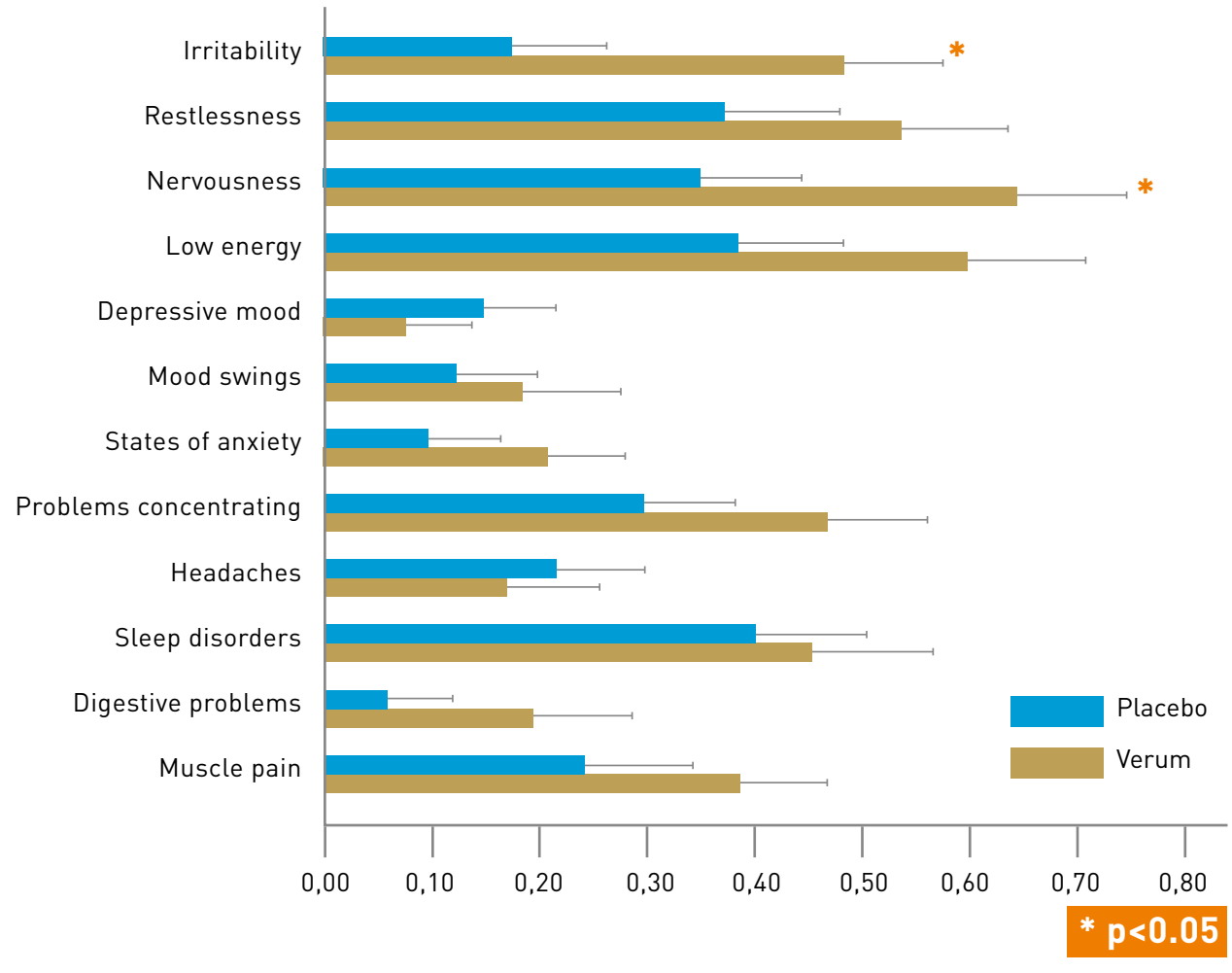
154 probands (70 % female, average age 53 years) with states of nervous exhaustion (ICD: F48.0 Neurasthenia) were investigated in a monocentric, randomized, double-blind clinical study. Over a time period of 6 weeks, the probands took a tablet (Neurodoron® or placebo) three times daily. The study protocol stipulated three examinations (baseline, 2 and 6 weeks later), at which mental state was assessed. Initially, the study analysis revealed no positive effect of Neurodoron®. As a result, daacro conducted a detailed exploratory analysis. Positive effects of Neurodoron® were able to be demonstrated on the symptom level in particular. On 10 of 12 scales, reduction of symptom severity was more pronounced in the Neurodoron® group than in the placebo group. Even the two most important symptoms, irritability and nervousness, decreased significantly in the Neurodoron® group, when compared to the placebo group.

Positive tendencies could also be found on further scales: During the intervention, the Neurodoron® group showed a significantly more pronounced increase of happiness and a significantly stronger improvement on the physical sum scale of the SF36.

Probands in the Neurodoron® group evaluated the substance's effect on the progression of symptoms significantly more often as "large to very large" than the placebo group. Independently, the physician also evaluated the effectiveness of the substance significantly more often as "good to very good" in the Neurodoron® group.

These results, which were only able to be revealed after a differentiated post-hoc analysis of the data, document the great importance of intraindividual data analyses – especially in the fields of naturopathy, nutritional supplements and herbal medicines.

Exhaustion symptom change between V1 and V3



Hufnagel,R., Bergtholdt, B., Hellhammer, J., Semaca, C. & Schnelle, M. Effects of Neurodoron® in patients with nervous exhaustion – Results from a randomized controlled clinical trial. European Journal of Integrative Medicine, 2016, 8, Supplement 1, p. 43.

VISIT OUR WEBSITES:

WWW.DAACRO.DE // WWW.STRESSZENTRUM-TRIER.DE // WWW.WERDEPROBAND.DE