



# Green oat extract: Mental health and cognitive function

Green oat preparations have traditionally been used to support mental health and cognitive function since medieval times. Using a bioassay-guided development approach the activity profile of green oat extracts can be substantiated for *Neuravena*, a wild green oat variety. Their selective effect on cerebral enzymes backed-up by convincing evidence from animal studies indicates a promising avenue for using these extracts as safe and natural ingredients for food supplements, nutraceuticals and functional foods targeted at balancing mood, improving learning performance and social intelligence as well as stress coping abilities.

In today's intensely competitive working environment, we make increasingly greater demands on ourselves in order to excel or simply survive. We work longer hours, cut down on vacation time, invest in further professional education while trying to balance family with work at the same time. No wonder this lifestyle can jeopardise our mental and emotional well-being: we feel stressed, tired and exhausted, have difficulty concentrating and suffer from mood changes.

A recent survey of industry decision makers in 30 countries by the consultancy Grant Thornton revealed that in the year 2005 executives felt even more stressed than in the previous year. But it is not only managers who are putting their mental health at risk. Students, mothers and senior citizens are affected as well. In the United States, almost a quarter of the general adult population has suffered from fatigue lasting two weeks or longer [1].

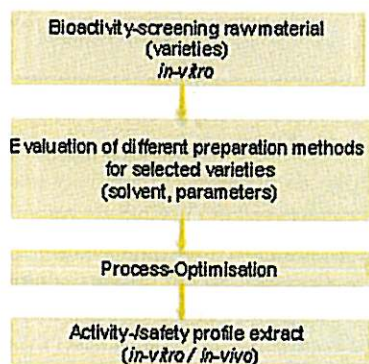


Figure 1. Rational extract development guided by bioassays.

In any given year worldwide 5.8 % of men and 9.8 % of women will experience a depressive episode [2]. In a recent European study, 13.6 % of European inhabitants reported a lifetime history of an anxiety disorder [3] and one new case of dementia is diagnosed every seven seconds [4].

### A growing market

Looking at these figures it is no surprise that the market for products aiming to improve mental health and cognitive function has been declared as emerging and promising in a recent report by analysts from Frost and Sullivan. The report identifies an untapped market for mental health products, particularly for memory enhancers, energisers and mood balancers. The target market is stressed-out individuals of twenty years old and above.

Pharmaceuticals have been the traditional first choice of consumers to alleviate mood swings, stress or cognitive impairment. But consumers are becoming wary due to possible side effects or effects of prolonged use. In contrast, herbal preparations are regarded as efficient, natural and safe alternatives to support mental and cognitive health, particularly for the treatment of mild cases.

### Rational extract development

Efficacy, safety and quality take centre stage in the botanical extract market. There is an increasing demand amongst formulators for ingredients with product-specific data in order to substantiate

possible claims. Common bibliographic data are becoming less important, since the pharmacological profile of different botanical extracts can vary drastically.

The clinical effect of a herbal extract cannot be attributed to any one single substance but is the result of the synergistic interplay of all constituents. The genetic and phenotypic variability of a plant as well as the extraction and extract refining technology used for the development of a multicomponent botanical extract are critical to maximise the health benefits and minimise the side-effects of the final product [5].

Bioassay-guided development is a state-of-the-art research method for the rational development of efficient and safe herbal extracts. The impact of different plant varieties as well as different extract preparation methods can be assessed by screening the bioactivity profile of an extract from the raw material up to the final product in *in-vitro* test systems connected to the target indication [Figure 1]. Similarly, safety and tolerance aspects of concern such as liver toxicity or enzyme interfering properties (e.g. cytochrome P450 oxygenases), which are important for determining the drug interaction potential, can be monitored. Hence, bioassay-guided development is not only

used to substantiate traditional or new areas of indication. It is also a scientific basis for the rational selection of the raw material and process technology best suited to design a safe and efficient herbal extract.

### Green oat – much more than a grain!

Preparations of the aerial parts of green oat have traditionally been used in popular medicine to support mental health and cognitive function since medieval times. Numerous sources praise the tonifying, stimulating, mood balancing and nerve strengthening properties of *Avena sativa* L. Hildegard von Bingen (1098-1179), the great medieval healer, for example, reported that the herb contributes to a cheerful and sharp mind [6]. The German Commission E monograph summarises uses of green oat preparations as follows: acute and chronic anxiety, stress and excitatory states, in cases of nervous exhaustion and as a tonic and restorative. The herb is safe and well tolerated at therapeutic dosages [7].

There are a handful of green oat preparations available on the market, targeting the traditional indications mentioned above. But currently, oats are primarily used for nutritional and dietary purposes, serving as breakfast cereal or a value-adding ingredient in bakery products.

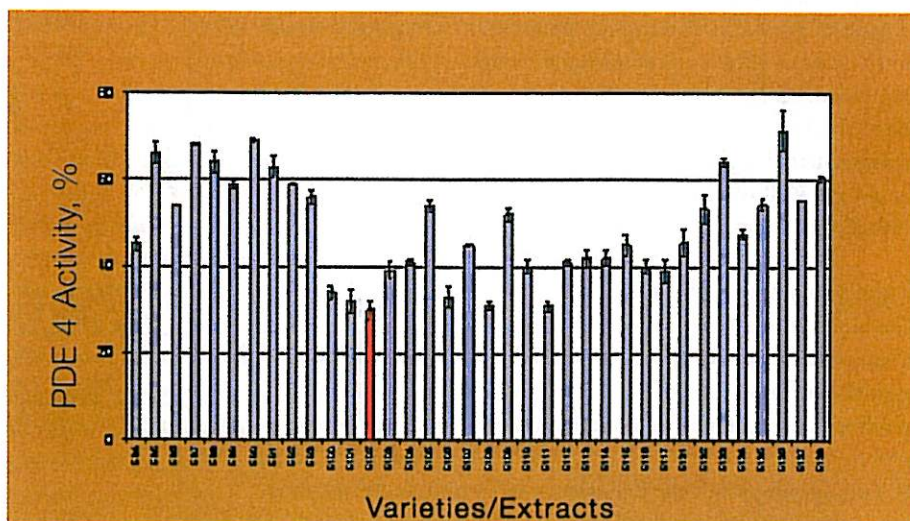


Figure 2. Differences in bioactivity in the PDE 4 bioassay. Inhibitory effect of different varieties of *Avena sativa* L. on PDE 4 activity in percent. (Extract concentration: 50 microg/mL) Red: *Neuravena* [8].

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consistent quality of raw material. The commercial result of this development is the patented wild green oat extract Neuravena (EFLA 955).

## Dual activity profile on mental health and cognitive function

The dual activity profile of bioactivity-tested green oat extracts on the CNS enzymes MAO-B and PDE 4 provides a reliable pharmacological basis to confirm the traditional indication profile of green oat extracts. MAO-B is responsible for metabolising dopamine (DA).

The levels of this neurotransmitter in the brain are important for the regulation of mental and cognitive function. Inhibitors of MAO-B are being used for the treatment of neurodegenerative disorders such as Parkinson's and Alzheimer's disease. The inhibition of MAO-B is associated with stimulant, mood enhancing and potentially neuroprotective properties [9]. PDE 4, on the other hand, is responsible for the degradation of the key second messenger molecule cAMP (cyclic adenosine monophosphate). cAMP allows intracellular signal transduction, i.e. for transferring the effects of neurotransmitters like noradrenaline. PDE 4 inhibitors increase cAMP levels in the brain, acting as signal enhancers. They are currently being investigated in clinical research for treating depression and for their role in cognitive enhancement [10, 11].

## Screening for evidence

In line with the drive for safety and quality and using a bioassay-guided development approach, the beneficial effect of green oat on mental health and cognitive function was recently substantiated by the Swiss extract manufacturer Frutarom for a selected wild type variety. Dozens of different varieties of *Avena sativa L.* were screened for their activity in various Central Nervous System (CNS) test systems, focusing on different targets connected to the traditional areas of usage of green oat. The current trend in primary usage of oats for nutritional and dietary purposes has led to the breeding of strains that produce high yields of carbohydrates rather than high levels of the medically important secondary plant metabolites such as flavonoids or steroid saponines. Therefore, the activity screening focused on old and wild type varieties with a high secondary or 'traditional' substance profile.

## Raw material is key

The bioassay screenings revealed a clinically significant inhibitory effect on two enzymes closely connected to mental health and cognitive function, monoamine oxidase B (MAO-B) and phosphodiesterase 4 (PDE 4). Depending on the raw material used, the inhibitory activity on the two enzymes varied dramatically [Figure 2]. Further progress of the bioassay-oriented process development was based on the MAO-B and PDE 4 inhibition tests using the best performing green oat variety, Neuravena. Extraction procedures and key manufacturing parameters were evaluated to identify critical steps, while contract growing of the product ensured

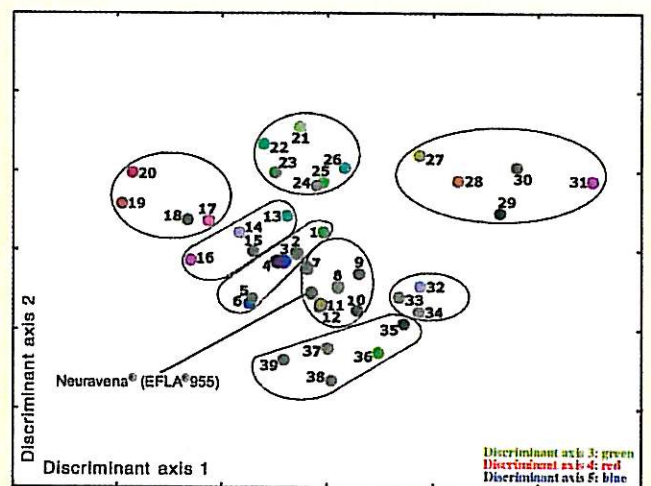


Figure 3. Classification of the electrical fingerprint induced by Neuravena in the "Tele-Stereo-EEG" test in comparison with reference substances representing the major indication areas in humans by means of discriminant analysis. #1-6: stimulating drugs; #7-12: antidementive drugs except for paroxetine (8); #13-16: analgesic drugs; #17-20: hallucinogenic drugs; #21-26: neuroleptic drugs; #27-31: sedative drugs; #32-34: anticonvulsant drugs; #35-39: antidepressive drugs. Neuravena is classified as similar to antidementive drugs [14].

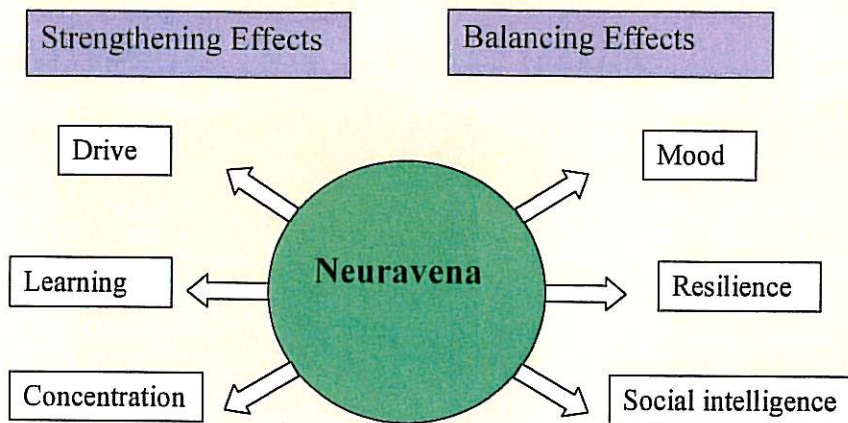


Figure 4. Dual activity profile of bioactivity tested green oat extracts.

### Exciting results of animal trials

In order to assess the activity profile of Neuravena in closer detail, the impact of the oral application of the extract on the electrical activity of the brain was investigated in freely moving rats. Using a continuous *in-vivo* analysis of brain field potentials ("Tele-Stereo-EEG") [12, 13], changes in brain field potential were recorded in four different brain regions for a group of four animals in a crossover design after oral administration. The extract was found to influence brain activity and to have stimulating properties. Neuravena seems to stimulate the dopaminergic (DA) transmitter system, which is implicated in cognitive functioning and motivation and is related to depression. In the model used in this study, the extract approached the results obtained from drugs used to treat dementia [Figure 3, 14].

Additionally, preliminary results of placebo controlled behavioural tests in rats investigating several CNS effects of Neuravena concluded that the extract improves general learning performance and speed of learning, ameliorates stress coping abilities and increases alertness. Moreover, test animals clearly demonstrated increased social interest and improved reaction to social signals, indicating a positive effect of the extract on an individual's soft skills; i.e. its social intelligence [14]. Complete results of this exciting animal behaviour trial will be published in the

course of this year. Findings of both *in-vivo* trials reveal a strong correlation with the pharmacological activity profile of Neuravena on MAO-B and PDE 4 found in the bioassay-guided development process, reinforcing mode of action as well as indications.

### Better moods and mental boosts

Given these consistent *in-vitro* and *in-vivo* findings, bioactivity-tested green oat extracts such as Neuravena may exert a strengthening as well as balancing effect on the brain and psyche, offering attractive positioning possibilities with regard to mental and cognitive functions.

There is strong evidence that the extract can support memory performance, help improve and speed up learning and memory function as well as improve an individual's social intelligence. Due to its stimulating effect it can help restore (mental) alertness and wakefulness - without the negative impacts of alternatives such as caffeine or ephedra. The extract, which has been thoroughly tested for safety and tolerance, can be positioned as a mood balancer, cognitive enhancer and booster of the individual's ability to socially interact, work under pressure and cope with stress.

### Bioactivity in focus

Looking at the evidence presented, bioactivity-tested green oat extracts are safe and natural new candidates for tapping the

emerging market of products that support mental health and cognitive functioning, provided the bioactivity of the final extract can be assured. The scientific selection of raw material and extraction technology using bioassay-guided development, as well as the consecutive contract growing of raw material, are key to assuring the bioactivity of the final product.

Using bioactivity-tested green oat extracts such as patented Neuravena (EFLA 955) manufacturers of food supplements, nutraceuticals or functional food are offered a new tool to add a mental and cognitive health dimension to their products and tap into a promising new market.

### References

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