

The world of micronutrients

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About the importance of an optimal nutrient supply for health, the potential of micronutrients in prevention and therapy, and the most important quality characteristics of high-quality dietary supplements.

What is an optimal supply of nutrients?

Our body is a finely balanced and extremely complex system of countless biochemical and bioenergetic reactions. Under ideal conditions, all these reactions interact perfectly to produce maximum vitality and health. The often expressed naturopathic view that the body is a self-healing system is basically correct, but it needs external support in many stressful situations.

Above all, the body needs a whole range of important ingredients to perform its daily miracle: these include fresh air, sleep, exercise, but especially so-called essential nutrients. Only an optimal supply of all essential nutrients enables all processes in our body to run as intended. The absence of one or more nutrients has far-reaching systemic consequences, since all individual biochemical reactions in our body are interconnected like a large network.

But what is an “optimal” supply of nutrients anyway? And when should we speak of a deficiency?

Essential and conditionally essential nutrients

In the first instance, a lack of essential nutrients may occur. These are vitamins, minerals, trace elements and other vital substances that the body cannot produce on its own and which it needs daily in certain quantities for survival.

However, there is a whole range of other nutrients that we can describe as “conditionally essential”. This means that the body is normally able to produce these compounds itself, but many people do not actually produce optimal amounts and urgently need an additional supply in the form of food. Examples of such conditionally essential nutrients are L-carnitine, alpha-lipoic acid, betaine, chondroitin, coenzyme Q10, choline and amino acids such as tyrosine or arginine.

Production of almost all these conditionally essential nutrients declines rapidly with age, which is why older people in particular can benefit greatly from supplementation. But even healthy young people do not always produce sufficient amounts of these conditionally essential nutrients. This is because a sufficient supply of essential nutrients is a prerequisite for these substances to be synthesised. If the supply of minerals or vitamins is insufficient, important enzymes do not function optimally and the

synthesis of the corresponding substances is severely impaired. A further factor is widespread genetic mutations, which also influence the effectiveness of various important enzymes. These mutations often lead to a considerable increase in nutrient requirements in order to maintain the optimal function of the enzymes.

For example, about one third of all mutations in the gene of an enzyme result in the corresponding enzyme having a greatly reduced binding affinity for a coenzyme – resulting in the enzyme's reaction rate being lower. About 50 human genetic diseases caused by such defective enzymes can be cured or alleviated by the administration of high doses of the vitamin component of the corresponding coenzyme, which at least partially restores enzymatic activity. [1] Good examples are the enormously important B-vitamin-dependent enzymes such as MTHFR, FAD, PLP, NADPH and TPP.

Where this is not sufficient, conditionally essential nutrients must be administered directly to restore optimal functionality. In fact, for many people, nutrients that the body should actually produce itself are also essential.

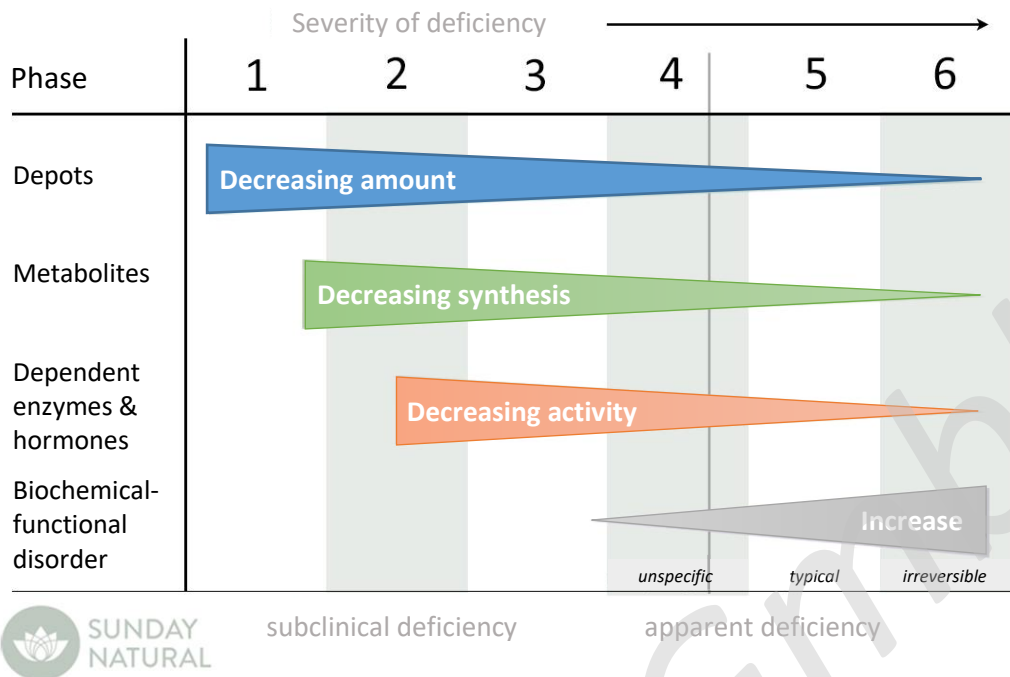
Definition of nutrient deficiency

The current view and definition of nutrient deficiencies presents some problems worth considering. To put it somewhat dramatically, one could say that what today is often regarded as the first clear indication of a specific nutrient deficiency is actually the last stage before irreversible damage occurs.

The majority of all nutrient deficiencies are subclinical and do not show any clear short-term symptoms at all. [2] And the reason for this is the intelligence of our bodies. In evolutionary terms, short-term nutrient deficiencies were always the reality for our ancestors. Our bodies have learned to compensate for this. Severe deficiency symptoms do not occur when the deficiency sets in, but only when compensation fails completely.

However, compensation is of course never an ideal state, as it comes with compromises. Small systemic errors accumulate until a point of decay or collapse is reached.

Perhaps you are familiar with the 6-stage system of nutrient deficiencies according to Brubacher, but I would like to introduce it briefly, as I will refer to it several times. [3]



6 stages according to Brubacher

1. In the first stage there is a latent deficiency, and here we are already leaving the area of ideal provision. At this stage, a suddenly increased need due to e.g. stress, exposure to environmental toxins, medication or an infection, depending on the nutrient, cannot always be covered, and the body can progress rapidly to later deficiency stages.
2. Nutrient-dependent enzymes and hormones can no longer be produced sufficiently as early as in the second stage, and so the body's systemic crisis begins to develop. This is already where the first impairments of bodily functions, greater susceptibility to illness and a reduced capacity to compensate for physical and psychological stress of any kind develop.
3. From the fourth stage on, the first clinical – but unspecific – general symptoms appear, such as fatigue, loss of performance, immune deficiency. The body's repair and detoxification functions are now greatly reduced.
4. It is only in the fifth stage that the physical symptoms are quite clearly due to a deficiency of a specific nutrient. Many diseases cannot be cured without remedying these deficiencies and often have to be treated with high doses.
5. Irreversible damage can occur in the sixth stage, which for some nutrients can also lead to death.

Problems with diagnosing nutrient deficiencies

But how is a nutrient deficiency defined? On the one hand, there is a clear symptomatic indication through the severe deficiency symptoms of the aforementioned 5th deficiency stage: scurvy with vitamin C, pellagra with vitamin B3, anaemia with vitamin B12 etc. However, this perspective is of course much too late.

Then, on the other hand, there is the assessment based on conventional blood values. These are also not unproblematic and are often not conclusive. For many nutrients

there is a drastic difference between cellular nutrient supply and blood levels in whole blood or serum. Blood levels do not necessarily reflect the actual status of the cellular supply – often the body has been in a state of deficiency for a long time by the time blood levels indicate this. Magnesium is a prominent example here - the blood values here are almost worthless and only intracellular levels provide information about the actual status of magnesium. [4]

Latent nutrient deficiencies often remain undetected in the early stages if a diagnosis relies entirely on nutrient levels in the blood. If we also take another look at the connections between genetic mutations and various enzymes discussed above, it becomes clear that optimal nutrient requirements are different for each person and are a highly individual matter. A deficiency is a functional disorder and this *cannot* be assessed on the basis of nutrient levels alone. The bandwidths here are enormous and general reference values provide at best only rough guidance.

Even if we briefly disregard this complexity, the threshold values themselves remain a problem. They are determined – in a rather simplified form – by looking at the blood level at which the severe deficiency symptoms disappear – or what the average blood level of a large number of apparently symptom-free people is.

However, neither approach gives us ideal blood levels, as we now know. Some of these definitions date back to a time when laboratory diagnostics and our systemic understanding were far from what we know today. Optimal blood levels should not be defined by the absence of symptoms, but by optimal functional activity of the corresponding nutrient.

Nowadays, it is often more effective to measure not just the nutrient concentrations themselves. This is because it is often possible to assess a really good supply situation much more accurately by measuring indirect markers or the levels of nutrient-dependent proteins and enzymes. It has been shown time and again that conventional blood levels do not provide reliable information about the actual cellular supply situation – and that the traditional thresholds are often set too low.

One example would be vitamin B12, which can be assessed much better with the help of indirect markers such as homocysteine and methylmalonic acid. These are substances that accumulate in the blood when there is a cellular vitamin B12 deficiency. Comparative studies show that secondary markers react much more sensitively than serum B12. Serum B12 often shows completely inconspicuous levels when cellular deficiency has long since been revealed by secondary markers. [5]

Triage theory: The danger of underlying nutrient deficiencies

Today, it is becoming increasingly clear to us that such “subclinical”, symptom-free deficiencies in stages 2 and 3 pose a high health risk in the long term – mainly due to the body's compensatory performance mentioned above.

Molecular biologist Professor Bruce Ames very effectively explained the possible connections in his triage theory. Triage is a term used in emergency medicine and describes a methodical procedure for prioritising medical assistance. Ames believes that the body has a very similar system of prioritising nutrients, with the major systems being supplied first. The triage theory states that in the case of a latent micronutrient

deficiency, the few available resources are initially used only for those bodily functions that directly ensure short-term survival – at the expense of severe long-term effects for the organism, of course.[6]

Even in the case of a significant micronutrient deficiency, the body uses this mechanism to ensure that the individual continues to function somehow at first – in evolutionary terms a highly intelligent adaptation. The body consequently down-regulates all functions that have more of a long-term benefit, such as ensuring the integrity of mitochondria, DNA and cells. It is precisely for these reasons, however, that sooner or later serious chronic diseases – and above all premature ageing – develop.

What happens here makes great evolutionary sense: the body trades long-term life for short-term survival. Damage to the mitochondria or DNA will inevitably have serious consequences in the distant future – nevertheless, it is more important for the body to first ensure short-term survival. From a biological point of view, it does not make sense to invest the limited resources that are available during a situation of scarcity in health in old age. In evolutionary terms, the only important thing is to maintain the body until it can reproduce.

The triage theory explains why the risk of chronic diseases increases so strongly with underlying nutrient deficiencies – even when the deficiency is not consciously perceived by humans as symptomatic. The body does everything it can to ensure that everything continues to function to some extent – but it borrows this “health” from the future.

Triage using the example of selenium

Professor Ames and his team were already able to show that this prioritisation is indeed the case with a number of nutrients. One of them is the trace element selenium. [7] Selenium is necessary for the synthesis of a whole range of proteins. These selenium-dependent proteins can be switched on and off more or less individually by certain genes. Experiments on what were termed knock-out (KO) mice, where one or more genes were deactivated (gene **knockout**) by means of a targeted genetic manipulation, made it possible to determine which of these selenium proteins are directly necessary for short-term survival – because the corresponding KO mice died within a short time or were unable to reproduce – and which of these proteins apparently have a more long-term benefit. Ames thus succeeded in establishing a hierarchy of selenoproteins ranging from vital and essential to insignificant and non-essential.

Studies on healthy mice have now shown that a selenium deficiency actually causes the body to produce almost exclusively essential selenium proteins – the body draws resources away from the less important proteins to ensure short-term survival. It is equally astonishing that when selenium was administered, the proteins responded again in almost the exact order of their hierarchy.

A latent selenium deficiency therefore does not exhibit any immediate, drastic symptoms – nevertheless, it may well be that the body no longer produces half of the selenium proteins in sufficient quantities, and this must have serious long-term consequences. Our body is therefore highly intelligent and capable of immense compensatory performance, which we at best are only just beginning to understand.

It is important for every therapist to recognise here that neither the absence of clinical symptoms nor sufficiently high blood levels automatically mean an ideal nutrient supply. Secondary and indirect markers are often necessary to reliably assess a supply situation. In addition, a check on all important nutrients is also recommended as part of every bioresonance anamnesis, since deficiencies can often be detected much earlier than they appear in the blood count.

Treatment versus prevention

At this point we should first make a central distinction that often leads to confusion: the difference between treatment and prevention. On the one hand, nutrients are important in the treatment of health problems, but on the other hand they are also the best prevention against a huge range of diseases and, if correctly dosed, completely without side effects. No medicine can make the same claim.

As we have seen above in our consideration of deficiency stages and the triage theory, latent nutrient deficiencies are a major risk factor for many diseases. Conversely, this also means that nutrients have an enormous preventive potential against all diseases of old age, chronic and immune diseases, diseases of civilisation (cardiovascular diseases), mental illnesses, metabolic diseases, cancer and many other disease patterns.

However, the preventive use of nutrients differs substantially in form and dosage from a therapeutic use. The aim here is an even, physiologically natural supply of all nutrients. This is best achieved by a long-term, steady intake in moderate doses. The nutrients are optimally from the most natural source possible and in combination with natural cofactors and plant substances. Basically, the aim here is to get as close as possible to the food model. Wherever possible, the use of real superfoods and other foods is clearly preferable to isolated nutrients. As a minimum, however, the natural, physiological forms of the nutrients should be used.

Therapeutic use differs significantly from this. Nutrients often have a *direct* effect on specific diseases – especially in deficiency stages 4-6. It is often necessary here to remedy deficiencies very quickly. The pharmacology of many nutrients – i.e. the interaction of bioavailability, half-lives in the body and metabolism – often requires extremely high pharmacological dosages. Nutrients can also be used here in a targeted manner to stimulate or suppress certain immune reactions, to initiate detoxification processes or to intervene in a similarly targeted manner in the biological system. Therapeutic use is usually characterised by a very high dosage of bioactive forms. These doses can often no longer be achieved with natural extracts. High-purity bioactive nutrients in pharmaceutical quality are therefore recommended here.

So let us take a look at both areas and the reasons for using nutrients.

Nutrients in treatment

Huge therapeutic benefits can be achieved through nutrition alone. And this is not surprising, as nutrients are the absolute cornerstone of our health. It is only possible to keep the body healthy if there is a sufficient supply of all essential nutrients. They are as essential for all immunological processes of the body as they are for renewal and detoxification processes.

In our experience, nutrients should therefore be a central – and obvious – component of every medical therapy. No exceptions.

There are numerous studies that show, for example, that surgery can be performed with fewer complications and the healing process can be accelerated if certain high-dose nutrients (for example, omega-3 fatty acids, arginine and nucleotides) are used prior to surgery to ensure that the patient has an optimal immune status. The effects were so clear that some meta-analyses recommend that preoperative nutrients should be included in the standard protocol for surgery [8]. Supplementation with a multi-nutrient solution also showed that important markers such as inflammation were significantly lower when patients received sufficient micronutrients prior to surgery. [9] This is all the more alarming when one considers that the average hospital meal can hardly serve as an example of holistic, wholesome health food.

In our view, similar benefits can be expected for all forms of therapeutic treatment when used competently – from physiotherapy to the treatment of simple infections and major surgery. In particular, however, nutrients undoubtedly play a very important role in the treatment of all more complex health issues such as chronic infections, autoimmune diseases, systemic disease patterns, toxin contamination or similar indications. Here we would go so far as to say that treatment without changes in dietary habits and a sensible, targeted nutrient therapy is unlikely to have any prospect of lasting success.

Disease = nutrient deficiency

Every health-related symptom is always accompanied by a lack of nutrients. It should of course be noted that this is not always a causal factor – on the contrary, a nutrient deficiency is often also the result of an increased nutrient requirement due to immune processes, parasites, poisonous stress or absorption disorders. Regardless of the question of what the causal connection may be, however, there is hardly a patient with clear symptoms who does not also have at least a few serious nutritional deficiencies.

The more we understand biochemically how deeply nutrients are involved in all healing processes, immune reactions and detoxification processes, the more obvious it becomes that it is of utmost importance to establish a state of sufficient nutrient supply for all recovery processes in order to optimally support the healing process. Nutrients are of enormous importance for *all* healing processes, directly or indirectly. They regulate the immune system and are necessary for repair processes. Healing and detoxification processes *always* consume large quantities of nutrients – nutrients should therefore always be used in a targeted manner.

However, the connection is much more significant than that. Many clinical pictures also lead to a considerably increased nutrient requirement in themselves, and this in very different ways. At this point, we would like to mention just a few salient examples that we hope will encourage you to think further.

Diseases such as cryptopyrroluria or haemopyrrolactamuria (HPU) lead to a greatly increased elimination of nutrients, which can cause real deficiencies. Those affected need nutrients in considerably higher doses than the official daily requirement in order to compensate for one of these deficits.[10]

Another underestimated problem is for example chronic exposure to pathogens or parasites. A disturbed intestinal flora – whether due to a bacterial imbalance, fungi or parasites – leads to a significantly poorer absorption of nutrients. [11-13] This leads to a kind of vicious circle: the further the disease progresses, the greater the impact on the nutrient balance and hence the body's immunocompetence. Incidentally, the same applies to all inflammatory bowel diseases, which also lead to a significantly restricted intake of nutrients. [14] Food allergies or sensitivities to gluten, fructose or lectins also frequently lead to a compromised intestinal flora and a correspondingly increased nutrient requirement. Genetic deficiencies in certain enzymes can also lead to food not being digested properly and nutrients not being utilised sufficiently. [15]

A fascinating area is also that of chronic infections, such as Lyme disease or Epstein-Barr. We need to remember that these pathogens have evolved alongside humans. Pathogens not only develop resistance to drugs such as antibiotics, they have also developed extremely clever survival strategies against the human immune system in the course of evolution.

The Epstein-Barr virus is particularly clever in this respect. EBV can specifically inhibit various immune reactions that might be dangerous to it – for example, an EBV protein blocks vitamin D receptors to prevent the release of antiviral immune substances. [16] Vitamin D remains partially ineffective here, which is critical especially when vitamin D levels are low anyway. Sufficient vitamin D levels should be ensured, especially with EBV, since EBV proteins and vitamin D compete for the VD receptors. Incidentally, a simultaneous EBV infection with a vitamin D deficiency is now regarded as the central trigger for multiple sclerosis. [17] At the same time, EBV disrupts the immune response by influencing immune messenger substances. [18] EBV can thus hide in tissues because it can largely paralyse the intracellular immune response. Semi-essential nutrients such as glutathione, for example, can help here. On the one hand, it is the most important cellular antioxidant and, on the other, it is a kind of messenger substance that mainly controls the intracellular TH1 immune reaction. Interestingly, studies have shown that high-dose administration of glutathione can completely restore the TH1 immune reaction, which means that pathogens can be combated again. The direct administration of glutathione bypasses the blocking by viruses such as Epstein-Barr, herpes and HIV and restores the immune balance. [19-23] A whole field of research is currently opening up in this area, revealing extremely interesting approaches for nutrient therapy.

As discussed above, a large number of diseases may also have a strong genetic component that affects one or more metabolic pathways. These genetic mutations reduce

the activity and binding capacity of certain enzymes. As a result, the body requires much higher doses of the nutrients that act as a coenzyme to maintain full functionality. The new research field of nutrigenomics is increasingly showing that the nutritional requirements of individual people can vary greatly. [24, 25]

For many mental illnesses, for example, it is suspected that they could be substantially related to an MTHFR mutation, which interrupts the folate metabolism. About 10-15 % of the population has a pure MTHFR mutation that reduces the formation of active methyl folate by up to 70 %. The consequence of this is that, firstly, too little S-adenosyl methionine is formed, which as a methyl transmitter is essentially involved in the synthesis of many hormones and neurotransmitters and, secondly, the level of the cell toxin homocysteine rises sharply, which promotes cardiovascular diseases. A high dose of methyl folate, vitamin B12 and vitamin B6 can successfully compensate for this genetic defect.

Nutrients in prevention

While treatment is highly targeted and highly dosed, prevention is primarily aimed at ensuring adequate basic provision. Multi-nutrient preparations that provide all essential nutrients in sufficient doses are suitable for this purpose.

However, an important qualification must be made here. Every dietary supplement must bear the statement “Not a substitute for a balanced and varied diet”. Although many EU requirements are often a nuisance for us as manufacturers of dietary supplements, we agree 100 % with this statement.

As a general principle, nutrient medicine has a very holistic and systemic approach, as the biochemistry of the body cannot be considered in any other way. Nevertheless, it is always important to remember that nutrients have a fundamentally different effect than drugs on the one hand – something that is still not taken into account when designing nutrient studies [26] – and, on the other hand, food.

Dietary supplements can only be regarded as foodstuffs to a limited extent. Isolated nutrients do not occur in nature. And there is no nutrient that works in complete isolation, either. Nutrients always act systemically and in combination with a whole range of cofactors; they are the subject of finely balanced regulating loops and feedback systems. Human biochemistry is a systemic whole and whenever we think we can look at a part of it in isolation, we eventually find it connected to all other parts by fine threads. Nutritional medicine is naturopathy in its most original form. However, it also calls for a natural, systemic view, a good understanding of relationships, balances, nutrient interactions and sensible dosages.

So if we really want to take a holistic view of the issue, we have to acknowledge that natural foods never supply individual nutrients, but always nutrient compounds, embedded in a matrix of often hundreds of vital and plant substances. Today we know that natural foods contain a whole range of other ingredients such as secondary plant substances. The more we learn about these substances, the less “secondary” they

appear. [27] We do not even know many of these substances, while we only understand the effects of others to a limited extent. However, it is clear that almost all these substances have considerable health effects. Seen in evolutionary terms, these substances were part of our diet for thousands of years and it is probably not too far-fetched to assume that we have to regard these vital substances (i.e. life substances) almost as nutrients. A healthy, varied diet rich in fibre and secondary plant substances is therefore indeed the essential basis for the supply of nutrients.

Prevention: why DS?

Do we then need preventive dietary supplements at all? If you have followed media reports on the subject, you will have noticed that there is currently a major campaign against dietary supplements. Certain leading media usually describe them somewhere between pointless, often overdosed and dangerous. We have the experience of thousands of therapists worldwide who have used nutrients in a targeted and successful way in treatment. But what about prevention?

Preventive benefits can only be researched scientifically with extreme effort, since very long-term studies are necessary and causality is extremely difficult to clarify. Moreover, research here is still trapped in a pharmacological paradigm, which leads to incorrect study designs. "Does 1000 IUs of vitamin D reduce the risk of cardiovascular disease?" is a question that makes sense for a drug, but not for a nutrient. Here the question must be: "Does correcting a vitamin D deficiency with an individually required dosage reduce the risk of cardiovascular disease compared to people with a vitamin D deficit?" Test persons with a deficiency must therefore be selected and substituted in such a way that they achieve an individually optimal vitamin D supply, including the necessary cofactors. This is both complex and scarcely justifiable from an ethical point of view, as this would require a control group to be kept in nutrient deficiency for years. We therefore hardly believe that studies can be expected in the next 20 years that will allow definitive statements to be made in this regard. The methodological deficiencies are still too great and the topic too complex for simple answers.

Nevertheless, there are a number of good reasons for taking food supplements as a preventive measure, and I would like to briefly mention just four of them:

1. The nutrient content of our food is decreasing drastically

Not only do more and more people choose foods that have a very poor calorie/nutrient ratio, even our healthy foods contain fewer and fewer nutrients. [28] This is due to depleted soils, a disturbed "microbiome" in the soil and destructive cultivation methods, but also to the more easily cultivated varieties of many vegetables and fruits that are far removed from their wild ancestors.

Climate change is also making a contribution, as recent research shows. The higher concentration of CO₂ is shifting the internal balance of plants away from minerals, vitamins and phytochemicals towards more carbohydrates, which is contributing to an ever lower density of nutrients. [29]

The nutrient loss of our vegetables since the 1940s is estimated to be around 10-40 %. Needless to say, it is unlikely that 40 % more fresh vegetables have been eaten since that time, which could compensate for this loss.

The same can be observed for animal products and meat.

The loss becomes even more drastic if we take an evolutionary perspective. This is because the diet of a Stone Age man was probably many times more nutritious than the diet in the 1940s, which is our last point of reference. Our bodies are biologically and evolutionarily designed for a much higher nutrient density. [30] Dietary supplements can therefore – as their name suggests – close the ever widening gap between our actual biological needs and our daily diet.

2. Stress and modern lifestyle are increasing nutrient requirements

Emotional and physical stress considerably raise nutrient requirements. Whereas stress has always been part of human life, modern lifestyles lead to a kind of chronic stress load and, as a consequence, to a significantly increased need for nutrients. [31, 32]

3. Increased exposure to toxins is raising the need for nutrients

Humans today are exposed to a whole arsenal of pollutants and toxins – from softeners in our drinking water to the pesticides in our vegetables, from heavy metals in fish and plants to nanoparticles in our toothpaste and additives in dietary supplements – all of which have been proven to have a profound effect on our biology. These toxins and noxious substances not only lead to metabolic disorders, but their elimination and control also demand a certain amount of nutrient reserves from the body. Mercury and other heavy metals for example rob large amounts of iron, copper, vitamins B1, B2, B6, E, selenium, zinc and many others. The consequence here too is a significantly increased need for nutrients that are important for detoxification and the immune system. [33-36]

4. Medicines

About half of the German population take medication every day, and about a quarter of them take more than three or more drugs simultaneously. What many people are not aware of is that medicines are extreme nutrient thieves and lead to considerable additional requirements. One of the major nutrient thieves is the birth control pill, which is taken by about half of all young women. Every long-term treatment with medication should therefore be accompanied by selected micronutrients. [37]

Class of medicine	Leads to additional demand for
Birth control pill	Vitamin B1, B2, B6, folic acid, B12, vitamin C, zinc, iodine, magnesium
Acetylsalicylic acid ASA	Vitamin C, vitamin E, glutathione, SOD, folic acid, vitamin B12
Statins	Coenzyme Q10, selenium
Proton pump inhibitors	Vitamin B12, calcium, vitamin D, vitamin C, folic acid, magnesium
Beta blockers	Q10, niacin, vitamin B2, magnesium
Cortisone	Calcium, vitamin D, vitamin K, zinc, vitamin C, magnesium, potassium
Diuretics	Magnesium, potassium, calcium, vitamin C, vitamin B1, folic acid

Food supplements for prevention: as natural as possible

As outlined above, there is a clear difference between a natural nutrient supply from natural food and plant extracts on the one hand and isolated individual nutrients on the other.

We can basically distinguish between three major areas:

1. Superfoods

Special foods with high nutrient content (from the best terroir, special varieties, gentle processing, certified organic). – *Ideal for a basic supply of nutrients and plant substances in a natural, synergetic compound*

2. Natural plant extract

Embedded in a natural compound (ideally extracted without chemical solvents, with water and/or food alcohol only) – *Ideal for mild deficiencies or increased requirements, through targeted concentration of certain nutrients in slightly higher doses.*

3. Bioidentical synthetic active substance

As pure substance in pure pharmaceutical quality. – *Ideal for existing deficiencies and for targeted, high-dose treatment.*

We try to cover all these three areas for each nutrient, as they also represent different treatment scenarios for us and allow different dosages and technical possibilities. Unfortunately, this is not possible for the entire range, as we are subject to strict legal constraints. Many plant extracts that could provide wonderfully natural nutrients fall under the Novel Food Act and may not be used. Some physiological forms are also not approved as active substances.

A fourth category is actually purely synthetic artificial products, i.e. non-physiological active ingredients without direct biological effect. These substances cannot be found in nature at all, but have been used in food supplements for years because they are easy to produce and highly stable. We only make very careful use of these substances in a few cases, e.g. when no other active substances are approved and when we cannot achieve a similar, sometimes necessary high concentration by any other means.

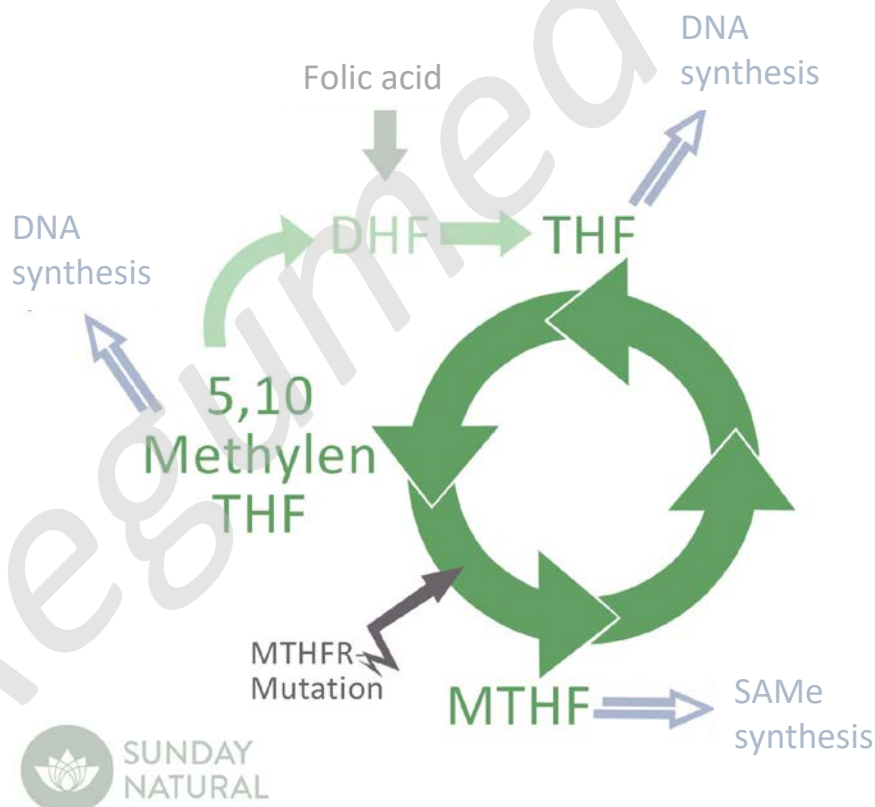
Example: natural folate complex

Let's take a brief look at the example of folate to make this even more illustrative.

Conventional *folic acid* is a purely synthetic substance that does not occur naturally in food or in our body at any time. To be utilised by the body, folic acid must first be converted into folate, more precisely into dihydrofolate or DHF. In our opinion, artificial folic acid should generally be avoided, as it can accumulate in the body and mask other nutrient deficiencies. It can also not be easily digested by many people.

A physiological alternative would be methyl folate (MTHF). This bioactive form of folate would be a highly effective synthetic agent that provides biologically identical folate, as it occurs in our body and food. [38]

Methyl folate is part of the folate cycle, a cyclic metabolic pathway of four different chemical forms of folate. Methyl folate is undoubtedly an important form in this cycle, but other forms such as 5,10-methylene THF also have important functions.



Natural folate, such as extracts from lemon peel, which are very rich in folates, usually contain all the folate forms of the folate cycle – i.e. they correspond to an entire folate complex. The typical distribution here is:[39]

- MTHF = (45 - 65 %),
- 5-formyl-THF = (30 - 55 %)
- THF and 5,10-methylene-THF = (10 - 15 %)

While a high-dose synthetic preparation would provide 100 % pure 5-MTHF here, a natural plant extract provides all forms of folate simultaneously.

Both have advantages and disadvantages. High-dose synthetic 5-MTHF is recommended in cases where the methylation cycle needs to be specifically modified or in cases of certain genetic defects such as the MTHFR mutation. For general care and especially during pregnancy, however, natural folate would be much more suitable, as it is precisely here that the effects of folate on cell division, which are mediated via 5,10-methylene-THF, should be promoted.

In a nutshell, one could say that isolated, high-dose nutrients allow greater influence and selective effects, while natural extracts tend to have a holistic-systemic effect and are usually more suitable for general prevention.

Depending on the application, different forms of folate or compounds of all the important forms of folate can therefore make sense. Our product range is structured accordingly. Therapists have reported to us that, even with the pure methyl folate active ingredients, the two best active ingredients Quatrefolic® and Magnafolat Pro® have different effects and compatibilities, which is why we now use both substances in our preparations and even combine them.

Summary: the importance of nutrients

So far we have looked at the course and health significance of nutrient deficiencies and have shown that latent, subclinical deficiencies also represent a significant health risk. We have discussed that nutrients are suitable for both prevention and treatment and explained why they can provide important services in both cases. We have also looked at the difference between natural foods or natural composite nutrients and isolated nutrients and derived some guidelines for food supplements from this.

Tips for everyday practice

What does all this mean in practice?

On the one hand, it must be acknowledged that the nutrient balance in the body is a highly complex matter that is not easy to test. A complete, laboratory-based nutrient check, which includes the 30 - 50 most important nutrients as well as their most important metabolites and secondary markers, can easily cost the patient a four-figure amount in euros. This is only likely to be possible and feasible for very few people.

On the other hand, interpreting these laboratory values is almost a discipline in its own right, as the individual parameters can only be interpreted meaningfully in context and on the basis of a good knowledge of the biochemical relationships. It requires a certain degree of learning to acquire this expertise.

Unfortunately, testing by bioresonance is also not as easy as one might assume, as has been shown in practice. Here it very much depends on the substance used for testing. Sometimes ready-to-use capsules are used, which distorts the results, as the body also reacts to the added substances. Tests must therefore be conducted with pure substances. Here, in turn, there are often innumerable forms available in countless qualities. Our own tests for optimising our blends have shown that a person's nutrient requirements can vary significantly throughout the day. And this not only when considered as a whole, but also especially with regard to individual active ingredients and forms of nutrients. A one-off test does not produce a clear result here, which is why we conduct long series of tests with several test persons to design our opti-compounds and then compile the compounds on the basis of statistical values.

All these factors form a real obstacle and are likely to contribute to the fact that many therapists are unsure and hesitant about the topic of nutrients, as confirmed by the feedback from many doctors and naturopaths cooperating with us.

Many therapists decide not to prescribe any nutrients at all or act on suspicion because extensive testing is not always possible. Neither situation is ideal. In the first case the disadvantage is obvious, in the second case there are justified reservations against giving high doses of nutrients purely on the basis of suspicion. A good third option here is a moderate basic supply of the most important nutrients. However, there are also understandable reservations about the multivitamin preparations, which are often put together indiscriminately or following the motto "the more, the better". Nevertheless, it is equally unreasonable for patients to compose a suitable compound of 70 individual preparations themselves.

We try to solve this problem together with selected therapists using a modular approach: The Sunday Essentials. The basic idea is to start replenishing the nutrients in parallel to the treatment, following a 3-step modular approach that provides basic support even without extensive laboratory diagnostics.

1. Multi-nutrients as the basis
2. Compound for special health aspects
3. High-dose individual active ingredients for a targeted effect

1. Multi-nutrients as the basis

In almost all cases it makes sense to use a multi-nutrient preparation as a basic supply that provides the most important 70 to 90 nutrients in moderate doses and a finely tuned ratio. A number of different aspects must be taken into account. First, the ratios of nutrients to each other must be proportionate and harmonious in order to avoid imbalances. Second, multi-nutrient preparations have the problem that many nutrients interfere with each other in the way they are absorbed. This can be circumvented by taking the nutrients at different times of the day and by using active ingredients that are absorbed by the body via different transporter systems and so do not interfere with each other. We take both approaches. Third, the body should be offered a rich variety of forms of bioactive substances, following the example of foodstuffs. We therefore compose our compounds entirely from the hand-picked premium active ingredients of our individual preparations. Fourth, the nutrients should be embedded in a matrix of high-quality plant substances that enhance and complement the overall effect. Depending on requirements, compounds with different dosages are advisable: fairly moderate for the normal basic supply, high dosages for increased requirements. This covers basic nutrient requirements and equips the body optimally for the additional needs of repair, elimination and healing processes. The simultaneous supply of the most important nutrients prevents gross imbalances in the nutrient balance and closes major supply gaps.

2. Compounds for special health aspects

There are also a number of nutrients for each health aspect that can support the healing process in a particular way or for which there is a significant additional need. These sometimes special vital substances and nutrients should therefore be given in higher doses in addition to a basic supply. Our goal here is to develop modular nutrient compounds, each in cooperation with experienced therapists, to be taken in addition to basic requirements. These compounds supply all nutrients in combination with their main active partners, cofactors and synergetic substances, so that a specific system can be addressed in a holistic and balanced manner.

One of Sunday Natural's goals for 2020 is to design compounds that are ideal for the most important fields of application and that can be easily tested and used in conjunction with treatment. At the end of this presentation, I would like to give you a brief outlook of this project, which we are undertaking in close cooperation with numerous therapists, and invite you to support us in this endeavour.

3. High-dose individual active ingredients for a targeted effect

In our opinion, the use of high-dose individual substances is only really meaningful with

appropriate laboratory diagnostics or with a precise knowledge of the facts. Even when

nutrients are in principle virtually free of side effects, high doses of individual nutrients can lead to imbalances and incorrect regulation. This can even lead to indirect deficiencies if important cofactors are missing at the same time. High-dose individual substances are

useful where the patient's nutrient status is precisely known and serious deficiencies have been identified in the laboratory that can be quickly remedied. They can also be used where certain response pathways – such as methylation – are to be deliberately addressed.

This three-step approach simplifies the use of nutrients during treatment and can optimally support recovery processes.

Quality characteristics of dietary supplements

In the following second part we would like to take a close look at the heart of dietary supplements and explain what actually determines quality, how big differences really are and what important recommendations should be observed in practice.

So if we have hopefully been able to convince you so far that nutrients can make an important contribution to prevention as well as to therapeutic practice, we would now like to describe what you should look out for when choosing appropriate preparations. As a manufacturer, we regularly test raw materials, sample the market and pay close attention to quality criteria and technical purity. Even we receive a lot of information only after extensive research and comparison, enquiries, visits to suppliers and laboratory tests for active substances and residues. The range of quality here is extremely wide, much wider than we ourselves ever expected. After all our experience as well as on the basis of many published studies, own laboratory tests and statements of our quality suppliers, who critically observe the market, we can conclude that:

1. Many preparations do not contain the dosages indicated on the label
2. Many preparations contain inferior, only partially effective active ingredients – or even no active ingredient at all
3. Many preparations use only single synthetic substances
4. Many preparations contain substances that do not even have to appear on the label (hidden additives, as they are technical additives such as nano-particles).
5. Many preparations are contaminated and manufactured under questionable conditions.

Let's begin at the end.

Purity: additives

One of our highest principles is purity. This means several things. First of all, it is our firm belief that a dietary supplement should wherever possible contain only the active ingredient and natural composite factors. All flavourings, colourings, preservatives and technical additives should be avoided whenever possible, especially if they are synthetic or produced by chemical means. Many of these widespread and supposedly harmless substances contain nanoparticles, affect the immune system or damage intestinal flora. They are at best useless.

It was a long process for our manufacturers to do without these substances, especially in the production of tablets. Even so, it is perfectly possible, even if it requires a little more expertise. We believe that in most cases today there is absolutely no reason to use food supplements with additives and your patients should not do so either.

Even supposedly harmless additives such as the filler microcrystalline cellulose may pose risks. Microcrystalline cellulose (MCC) may legally contain up to 10 % nanoparticles, which can pass through the intestinal wall and into the blood as a result of persistence. These are billions and billions of particles, even in the case of a just a few milligrams. Such an MCC may even call itself nanoparticle-free under EU law. We do not yet fully know what this means in terms of health, but we do not recommend that you try to find out yourself.

After months of research, we have so far found only one manufacturer that offers guaranteed nanoparticle-free microcrystalline cellulose, which we use in some products for production-related reasons, for example because some tablets really cannot be pressed in any other way. There are more sensible options available as a pure filler, because the space in capsules can be used just as well for real food. One of the things we use is organic germinated buckwheat powder, which contains many nutrients and is therefore a much more sensible filler for our capsules.

Purity: hidden additives

What many people do not realise is that even a glance at the list of ingredients on the label does not tell them the whole truth about additives. Statutory provisions are currently such that only those additives which the producer has added itself or which are not regarded as technical additives need to be listed.

In many cases, however, the raw materials – the highly concentrated vitamin active ingredients, for example – already come with a whole range of additives, such as synthetic vitamin E, silicon dioxide and others. These do not have to be indicated on the label – unless the manufacturer voluntarily commits itself to a full declaration of all ingredients. So you can easily buy a dietary supplement that contains some additives of concern without having a single one of them on the label. Most manufacturers are looking for the easiest and most cost-effective production process, not the one that makes the most sense in terms of content, and many production processes can be significantly simplified and accelerated by the use of chemical auxiliaries.

Additives are also found in capsule shells, which are declared as pure cellulose (HPMC). In reality, however, they usually consist of more than just cellulose, as we have discovered. Almost all capsules on the market contain a whole range of dubious additives such as carrageenan and PEG. In our own cell study carried out with the Dartsch Scientific Institute on various capsule materials, we were able to show that these capsule shells have a considerable pro-inflammatory effect, whereas the ultrapure capsule shells without additives used by us do not show this effect. The situation is no different with softgels – here we had to go so far as to have our own capsule shells produced especially just for us, because we were simply unable to find any capsules on the market without hidden – and from our point of view questionable – additives.

Purity: contamination

A further aspect of purity is contamination. We should actually assume here that this should not be a major issue. Unfortunately, this is not the case. The fact that chemical contamination is not only a theoretical possibility but widespread reality is shown, for example, by the desperate attempts in professional sports to tackle this problem.

Over-the-counter dietary supplements are repeatedly presented as a source of illegal doping substances, hormones or even drugs. [40-44] The American Food and Drug Administration (FDA) found over 700 different products containing illegal substances through random sampling over a period of 10 years. A large proportion of these were apparently deliberately added, others contained the substances in minute concentrations, indicating contamination. [45]

This contamination is probably due to the fact that many dietary supplements share additives such as magnesium stearate with drugs or that raw materials are produced on the same machines.

While such contamination is of course hardly noticeable to the normal end user, in professional sport it regularly destroys careers, as the substances in question lead to positive doping tests. In many cases, however, the traces found can then be related to a special preparation.

Each additional additive increases the risk of such contamination. This is because the greater the number of different sources and production lines that go into the overall recipe, the greater the number of different sources of error. Of particular concern here are the additives from the stock of ever-present substances such as magnesium stearate and silicon dioxide, in most cases purchased in the cheapest quality.

Nevertheless, drug contamination is by no means the only problem: chemical solvents, heavy metals, bacteria and other toxic substances are also found in dietary supplements on a regular basis. [46-49] As we found, not even the analyses provided by the manufacturer can be relied upon in all cases – our own cross-checks with our partner laboratory showed considerable contamination with heavy metals and chemical solvents.

Ironically, the latter is an extremely common problem, especially with natural extracts. While ultrapure synthetic nutrients can easily be produced in pharmaceutical textbook quality, natural nutrients in particular require special attention. First, conventio-

nal cultivation can lead to an accumulation of pesticides and heavy metals, and second, genetically modified plants such as corn and soya can play a role. It is therefore recommended to use organic quality wherever possible or wild harvests from remote areas. We have started taking a close look at local geographical conditions even for organic qualities. Remote natural locations and protection afforded by mountains and forests are ideal, because pesticides from other fields can easily be blown in by the wind.

And third, natural extracts almost always use chemical solvents, traces of which can also be found in the end product. There is little point in using an extract from natural organic raw materials that contains residues of toxic solvents such as acetone, methanol and N-hexane. Extracts obtained from water and/or food grade alcohol offer the highest purity and should be preferred. They are significantly more expensive and more difficult to buy. We often have special products made for our extracts that are more expensive, but are only produced using safe substances. But not all ingredients can be extracted in this way.

The overall quality of raw materials is crucial. Today, the market is dominated by the cheapest possible raw materials, which are often offered by distributors and wholesalers from Asia. Laboratory analyses provided by the suppliers are often questionable and it is not uncommon for these suppliers to sell cheap qualities as supposedly high-quality, bioactive nutrients. Some purchasers do not carry out a final inspection. This is partly due to the fact that some manufacturers do not really want to know exactly because of the cheap price and the papers supplied. However, it is also due to the considerable costs of such tests, which are difficult to cover economically, especially for smaller manufacturers. Last but not least, there are only a small number of laboratory tests and laboratories that can test which forms and qualities of nutrients are really present in a sample. The overall trend in this area is rather negative, as the market for dietary supplements is now a billion-euro market and the price pressure, even among raw material manufacturers, is enormous. This is always bound to be at the expense of quality, as we will also see in other respects.

A large proportion of raw materials are now produced in Asia. This is not in itself a problem and some products and nutrients are explicitly only available in China and India in the highest quality. The general reputation "Made in Germany" or "Made in Europe" works very well in terms of advertising through association with the engineering and automotive industries, but is ultimately misleading. It is generally true that quality varies greatly in Asia, from premium quality to absolutely unacceptable quality. So for some products – such as our medicinal mushrooms – Asian countries may even be the best choice. In other areas we have in turn had extremely bad experience when comparing the Asian raw materials on offer. We therefore always select every single raw material individually solely on the basis of worldwide research from the best manufacturer in the highest quality. We frequently have materials produced to our own specifications in order to avoid the use of technical auxiliaries or additives.

Incidentally, the label "Made in Germany" or "German product" that you often find is not a reliable quality feature in other regards, either. It almost always refers merely to filling and capsuling, while the raw materials usually come from other countries. Even raw materials from Germany are not always the best choice in terms of quality and purity.

Nutrient content

Not only do many supplements contain a lot of things that should not be in them, but alarmingly they often do not contain what should be in them. Tests conducted by some of our well-known suppliers in the market and also numerous published studies have shown that many supplements do not contain the amounts of active ingredients indicated on the label. Some of the preparations tested even contained no active ingredient at all.

This problem has huge ramifications. They are so extensive that the large American pharmacy chain CVS announced that it would have all 1400 different NEMs from over 150 different manufacturers offered in its branches regularly analysed at its own expense in order to verify the claims on the label. [56]

The concerns are understandable. It is annoying if a preparation contains too little nutrient. If it contains far too much, it can even be dangerous, because if the actual dosage is much higher than the information on the label, this can lead to alarming overdoses of some nutrients.

For example, a large proportion of vitamin D preparations contain a completely different dosage from that stated on the label.

In two studies on this subject, only one third of the products tested achieved variance within acceptable tolerances. The content varied from only 10 % to 160 % of the reported dose in 75 % of the preparations. [50, 51]

In another study focusing entirely on products for children, 30 % of the products also deviated significantly from the claims, again with the actual content varying from 8 % to 177 % of the stated dosage. [52]

These huge variations are also caused by gross errors in production and are not without danger. Several case studies report severe vitamin D poisoning in children, and such errors regularly lead to life-threatening situations. [53, 54]

The situation is similar with the particularly expensive vitamin K2. Here too, various studies showed extreme deviations from the specifications on the label. One study found that a full third of the products contained *no* effective vitamin K2 at all, and the majority contained significantly less than claimed.

K2 is a good example, as this is a somewhat more complicated nutrient. Vitamin K2 exists in various forms, the most effective form being vitamin K2 MK7. This form also exists in two different geometric variants known as isomers: *cis*-K2-MK7 and *trans*-K2-MK7. It is only the *trans*-form that develops its full biological effect.

Active ingredients available on the market often contain a mixture of *cis*- and *trans*-MK7. However, only the *trans*-component is really effective. An active ingredient with a *cis*-content of 70 %, as is often found at present, would accordingly be only 30 % effective – of 100 µg, for example, only 30 µg would actually be active. So there is real labelling fraud here with regard to the *trans*-content.

One study in 2018 examined preparations with a proven all-*trans* content of 100 % and concluded that most preparations contained far more ineffective *cis*-K2 K7 than biologically active all-*trans*-K2. The actual *trans*-content was sometimes less than 25 %. The

study even found one product that contained no detectable active ingredient at all. [55]

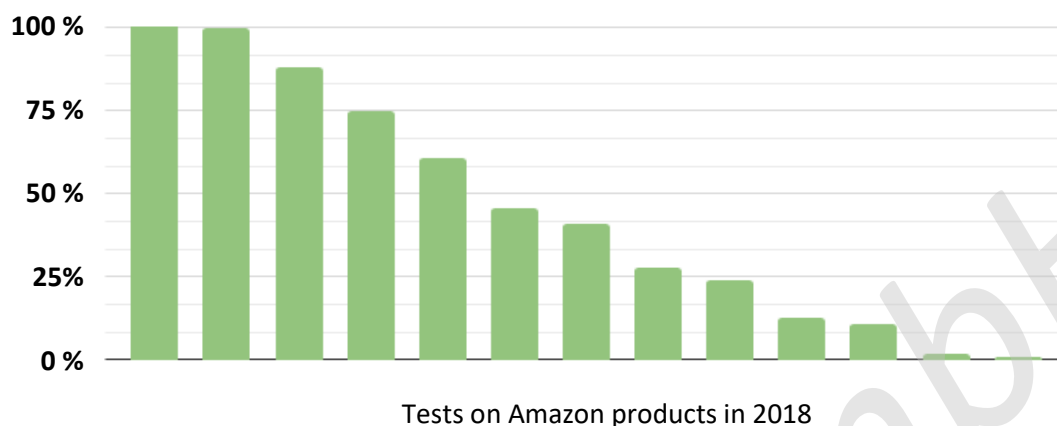
Tests of top sellers on Amazon.de

The 15 top sellers of vitamin K2 products on the Amazon.de sales platform were tested by an independent laboratory on behalf of one of our brand suppliers in 2018 in order to check whether observations made in US studies were applicable to the German market. The test results are presented here anonymously.

Manufac-turer	Reported con-tent of K2 MK7	Actual content of K2 MK7	Of which all-trans K2 MK7	Actual effec-tive K2
Xxxxxx	100 µg	61 µg	> 95 %	61 µg
Xxxxxx	50 µg	44 µg	> 95 %	44 µg
Xxxxxx	25 µg	25.1 µg	> 95 %	25 µg
Xxxxxx	19 µg	20 µg	> 95 %	20 µg
Xxxxxx	20 µg	15 µg	> 95 %	15 µg
Xxxxxx	200 µg	133 µg	69 %	91 µg
Xxxxxx	200 µg	74 µg	34 %	25 µg
Xxxxxx	100 µg	91 µg	31 %	28 µg
Xxxxxx	200 µg	305 µg	27 %	82 µg
Xxxxxx	100 µg	92 µg	27 %	24 µg
Xxxxxx	100 µg	58 µg	19 %	11 µg
Xxxxxx	100 µg	0 µg	0 %	0 µg
Xxxxxx	200 µg	0 µg	0 %	0 µg

Vitamin K2: How much does it really contain?

Active K2 as a percentage specified on the label



The test confirms the results of the above-mentioned studies: only a few products complied with the information on the label, most of them contained only a fraction of the indicated active ingredients, some preparations contained no active ingredient at all.

What is the reason for these large variations in quality?

I hope that by this point you have been able to understand that the production of supplements requires much more care and expertise than you might think. Losses occur for almost all nutrients during production and storage, and these need to be precisely calculated, compensated and verified by laboratory tests. Even very fast running machines can sometimes expose raw materials to high temperatures, which can also lead to nutrient loss, and that is why we only use slow running speeds in our production. Machines must be cleaned carefully and with safe agents to avoid any foreign matter, impurities and contamination. The problems described above result unless all this is done with the necessary care.

The majority of vitamin supplements today are not sold through pharmacies, therapists or reputable manufacturers, but through large international online mail order companies such as Amazon and eBay. These portals are today also used by simple “letterbox companies”. These companies sometimes do not even have a website, no premises, no or hardly any employees and have practically never held their own product in their hands. The preparations are produced and labelled according to the principle of “dropshipping” by a few large contract manufacturers, from where they are delivered directly to the warehouse of the online shipping department and sold through it.

It is estimated that about 50 percent of the supplements on major online sales portals such as Amazon and eBay are currently produced by a small handful of contract manufacturers – with different labels for different mailbox companies. This tactic was described a few years ago in one of the pertinent “getting rich on passive income” books and

has enjoyed great popularity ever since. It is not surprising that this approach is hardly likely to promise quality.

Major online mail order companies also have to struggle with plagiarism. A 2017 report by Forbes magazine revealed that about 25 % of the goods offered on Amazon.com that year were plagiarisms that could be traced back to China. [57] This problem from the tech and fashion sectors is also increasingly affecting dietary supplements, as recent alerts from Amazon itself showed when it warned its customers of counterfeit dietary supplements. [58] These products are indistinguishable from the original in terms of the product description and packaging for the end consumer.

These plagiarisms are possibly responsible for the repeated findings of absolutely drug-free preparations. However, it is also conceivable that cheap and faulty raw materials were simply processed without testing.

Natural & bioactive forms

We have discussed the purity and the active ingredient content, but an important quality aspect is of course the active ingredient itself. As shown in the example of vitamin K2, it is important to use the physiologically effective, bioactive forms wherever possible. Not all synthetic vitamin forms are as effective as their natural counterparts – for example because of the geometric isomers discussed.

What is more, the conversion of inactive, artificial precursors is often linked to metabolic costs. Enzymes are usually needed to convert these nutrients into their truly active forms, and coenzymes may be consumed. This transformation does not run smoothly in all people, also due to genetic factors. A good example of this is folate – around 30 % of the population has a genetic variant that greatly limits the conversion of folic acid into active methyl folate – in this case conventional folic acid is largely ineffective. [59-61]

On the other hand, many isolated active forms are not very stable and do not survive the gastrointestinal passage intact. In food, the active forms are protected because they are bound to carrier molecules such as proteins or fats. But they do not have this protection as an isolated material. In many cases, therefore, semi-synthetic active ingredients must be used, for example stable salts. Again, we can take folate as an example, where only methyl folate salts exhibit good availability. Although these salts do not occur even in nature, they release the natural and bioactive form of the vitamin in the body. Such an active ingredient is therefore bioidentical to natural forms despite its synthetic production.

Many nutrients have not just one, but a whole series of such natural and physiological forms, as we briefly touched on above using folate as an example. Further examples are: Vitamin B12, with two active coenzyme forms and three natural food forms [62-65] and selenium, which exists in a myriad of natural selenium compounds. In many cases all these forms have their biological function and justification here. Even if this cannot be clearly deduced scientifically in all cases, it can be assumed that a combination of many – or ideally all – natural compounds will result in an optimal supply. Stu-

dies showing, for example, the superiority of selenium yeast over individual active ingredients point in this direction – selenium yeast contains more than 20 different natural selenium compounds, including the particularly interesting selenocysteine. [66, 67]

Selenium yeast is also a good example of semi-natural nutrients. We talked above about the benefits of natural plant extracts. However, these are often very expensive and complex to produce. A compromise that is therefore often adopted is semi-natural nutrients. Here, a medium such as yeast or buckwheat is cultivated with a large surplus of nutrients. In the case of selenium yeast, for example, the yeast is cultivated in a solution with a high concentration of selenium or the buckwheat for our natural vitamin B complex is germinated in a nutrient solution with high doses of B vitamins. During the germination process, the buckwheat absorbs and metabolises the nutrients, converting most of them into their natural, physiological forms. When the buckwheat is harvested and the cells are broken down by grinding, highly available, natural nutrients are obtained in their active food forms. Although it is not possible to achieve high doses in this way, it is very easy to produce high-quality, natural nutrients, which can also be administered as pure food powder with the intact complex nutrient spectrum, and chemical extraction is not necessary.

Nutrients, cofactors, antagonists

We noted above that nutrients always work in a systemic context. Most nutrients depend on other cofactors for their effect and require certain coenzymes for conversion or metabolic steps.

The correction of a single nutrient deficiency can therefore lead to the increased consumption of cofactors and thus trigger an indirect cofactor deficiency. A nutrient cannot develop its full effectiveness if the cofactors are missing from the outset. Parallel administration is recommended in both cases.

Antagonists

The opposite of cofactors are antagonistic nutrients that hinder each other in their absorption and effect and which must be present in the body in a very specific ratio and balance. Here too, the substitution of individual substances can become problematic if they disturb the often sensitive equilibria.

For example, all bivalent metal ions are mutually inhibited against absorption, i.e. a high-dose administration of one of these substances inhibits the absorption of all others. [68, 69] Nature solved this problem in such a way that the body provides different transport routes for these substances. Various natural chelate forms are absorbed via alternative pathways such as amino acid transporters. Precise knowledge of the various uptake pathways and interactions is necessary in order to be able to compile meaningful nutrient compounds in this area. A clever combination of precisely selected active ingredients enables such antagonistic agents to be distributed to different transport systems in such a way that they no longer hinder each other.

Cofactor example of vitamin D3 homeostasis

A good example of the close interaction of cofactors is the vitamin D system. It is extremely complex and can only be greatly abridged and presented here in rudimentary form.

Vitamin D3 exists in the body in various chemical forms, the three most important of which are

- The vitamin form: vitamin D3 (cholecalciferol)
- The transport form: 25-hydroxyvitamin D3 (calcidiol)
- The hormone form: 1,25-dihydroxyvitamin D3 (calcitriol)

Magnesium

The conversion of the different forms into each other takes place with the help of special enzymes, the hydroxylases, which are magnesium-dependent. Magnesium deficiency means that the vitamin form cannot be sufficiently converted into the other two forms. [70, 71] This correlation is so strong that there are case studies where the 25-hydroxyvitamin D3 status could only be corrected by the administration of magnesium. [72-77] In this case, despite a low vitamin D level in the blood, further administration of vitamin D would not have led to the desired effect because the vitamin is locked in its metabolism.

Conversely, high-dose revitalisation with vitamin D can give a marginal magnesium level the last “push over the edge” and thus trigger magnesium deficiency. The connection between vitamin D and magnesium is therefore very close and joint intake is highly recommended.

Boron

The trace element boron also has an effect on hydroxylases – but this time on the degrading enzymes that in turn destroy the vitamin D storage form. It is only when both the formation and breakdown of 25-hydroxy-vitamin D3 take place in a controlled manner that the body can properly regulate vitamin D levels. A sufficient amount of boron is necessary here to avoid excessive decomposition of 25-OH-D3. [78] Similarly, it is important to prevent too high a calcitriol value or an unfavourable ratio between calcidiol and calcitriol.

Calcium

We now come to the most complex interaction. Vitamin D3 is necessary for calcium absorption in the intestines. If the level of calcium in the blood drops, more parathormone is released, which in turn boosts the conversion of vitamin D into the active vitamin D3 hormone. This causes four things:

- 1) It promotes calcium absorption in the intestines,
- 2) It dissolves calcium from the bones,
- 3) It increases the influx of calcium into cells,
- 4) It downregulates PTH again. [79]

Thus, if we have a calcium deficiency and at the same time a high vitamin D substitution, we have a very high level of PTH and at the same time a very high level of the active vitamin D hormone. This has more negative than positive consequences. On the positive side, it stimulates the absorption of calcium in the intestines, but on the negative side, the body begins to release calcium from the bones – although vitamin D is taken in high doses – and, even more worryingly, the influx of calcium into cells increases. The latter leads to severe cellular inflammation when PTH and calcitriol levels are chronically high. At the same time, the cell also starts pumping magnesium out to maintain a balance of electrolytes within the cell, which leads to intracellular magnesium deficiency.

As if this were not enough complexity, magnesium also regulates PTH levels. This means that both calcium and magnesium are necessary to properly regulate the parathyroid hormone and achieve a healthy vitamin D balance. [80, 81]

Practice shows here that there is an ideal ratio of active vitamin D hormone to 25-OH-D3, which can only be correctly adjusted by the simultaneous administration of vitamin D, calcium, magnesium and boron. [82]

Vitamin K2

Finally, there is vitamin K2. Although this vitamin plays no direct role in vitamin D metabolism itself, it does play a role in calcium metabolism. It ensures that calcium is removed from the blood and incorporated into bones. The calcification of tissues and organs can occur in the absence of K2 (MK7 alltrans), meaning that K2 is also a useful cofactor in this context. [83-86]

An ideal vitamin D supply takes these relationships into account and supplies all of the nutrients from this active complex. A good winter dosage could look like this, for example:

Nutrient	Dosage
Vitamin D	4000 IU
Calcium	750 mg
Magnesium	375 mg
Vitamin K2	200 µg
Boron	3 mg

Sunday Natural quality

We hope that this presentation has given you an idea of the complexity, but also the potential, of nutrients for therapeutic and preventive practice.

As a manufacturer of dietary supplements, the above-mentioned relationships require a high degree of expertise, research and attention to detail in order to design truly high-quality products. We would also like to make a contribution to achieving greater transparency in a very confusing market and really give our customers all the information they need to assess the quality. We are one of the few manufacturers that have committed themselves to a true clean label. This means that absolutely all ingredients are stated on the label, even if it is not obligatory to declare them. We also provide detailed information on the origin of the raw materials, their processing and the exact methods and means of production.

Every single nutrient in our range is handpicked and laboratory tested. In many cases, we need to have active ingredients made especially for us because the quality we require is not available on the market. We have had to team up with international specialist laboratories or universities for a number of active ingredients in order to obtain meaningful tests. For example, we have our vitamin K2 tested in a special laboratory in Norway and our OPC tested by Braunschweig Technical University, which is one of the few institutions that can individually determine the di- to pentamers that are mainly effective in the overall OPC and thus make a real quality statement possible. Such tests permit us to search specifically for the best active ingredients and to develop products such as our OPC Di-Tetra, which has the world's highest content of highly effective di- to tetramers.

We try to have both the most important individual active ingredients in our range as well as our specially adapted compounds of active ingredients. We always use natural foods and physiological relationships as a blueprint for our compounds, combining the natural forms in a specific ratio to achieve optimal effectiveness. In addition to the active ingredients, we also try to include cofactors, secondary plant compounds and complementary substances in order to increase absorption and tolerability.

All our compounds are our own formulations, which we put together ourselves from the individual high-quality active ingredients. Today there are many ready to use and very cheap compounds that can be bought from contract manufacturers, but they are of very poor quality.

We often spend months of research on our nutrient blends to find the optimal composition and to match the ingredients perfectly. The formulations are first of all developed and optimised by **bioresonance testing** on different people and secondly, as far as possible, verified in the laboratory by scientific cell studies. In 2019, we were thus able to impressively prove the superiority of our Magnesium Complex Ultra through extensive cell studies, which have since been published in a scientific journal.

Wherever we can, we use organic-quality active herbal ingredients. Where this is not an option, we use premium active ingredients of European pharmaceutical quality. All active ingredients are tested for residues and impurities.

We visit the farms that grow our tea and superfood products in order to gain our own impression of the production conditions and geographical location and to establish personal relationships with the producers. We try to find remote farms, if possible at high altitudes that are well protected by forests or mountains against external pollution. We also document for our customers how long a farm has been growing organic crops in order to make the quality of the soil traceable. In addition to qualitative and ecological aspects, we also pay particular attention to fair working conditions. We purchase all raw materials directly from the producers in order to be able to talk to them personally and negotiate fair prices for both sides through direct trade.

We produce on extra slow running machines in an organic factory to minimise nutrient losses through the influence of heat. We test the nutrient content of the finished product as a check. This is important because testing of the raw material alone does not provide information on whether the dosage and composition in the end product are correct and whether and how nutrient losses in the production process have to be compensated. Although this means an enormous financial and logistical effort, it is the only way to ensure the quality of the end products beyond any doubt.

When it comes to purity, we have now reached a level of detail that as far as we know is unrivalled, but which is almost impossible to communicate. We are working here on a comprehensive presentation of all our measures, which we will publish in mid-2020.

Apart from the raw materials, we now have our own capsule shells, high-purity glass packaging, special pollutant-free storage boxes in our distribution warehouse, sustainable, mineral-oil-free shipping packages, and we only use special food alcohol to clean the production machines.

We are currently working on energising our products by means of suitable processes and will also carry out cell studies to prove their effectiveness.

We are pleased to be able to offer all REGUMED therapists who share these values a cooperation agreement in which all your patients can receive our products at an attractive discount for the first two orders. We deliberately do not offer cooperation with therapists on a commission basis, as this seems ethically extremely questionable for us. Financial incentives could tempt therapists – similar to multi-level marketing – to recommend products even outside clear indications in order to make a profit. We therefore consider a direct discount for the end customer and a discount for the therapist's private consumption to be a better option.

Sunday Natural aims to produce dietary supplements with the highest possible efficacy and purity that are particularly suitable for use in a therapeutic context.

As already mentioned above, it is our goal to develop special nutrient compounds for all important symptom patterns in cooperation with experienced therapists that can be used in a supportive way in treatment. If you are interested in cooperation, we would be very pleased to hear from you.

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