

MUSHROOMS.

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In Buddhism and Grecian science there were four elements: earth, fire, air and water. In Japanese culture there was a set of five elements: earth (地), water (水), fire (火), wind (風) and void (空): go dai, "the five great" (五大). Until the end of the era of alchemy it was believed that these four elements made up the realms of the cosmos wherein all things exist and whereof all things consist. According to Paracelsus the most important of the elemental spirits of the element "earth" are gnomes and goblins. Gnomes are usually kind creatures, goblins are mostly evil. Goblin women steal human babies and dump them, replacing them with ugly goblin babies (changelings). Changelings were always burdened with severe birth defects such as spina bifida, cystic fibrosis or homocystinuria.

Gnomes are living deep underground guarding buried treasure. It is therefore not a surprise that a large number of bankers are gnomes, usually kind people if you don't need them, sometimes referred to as the "Gnomes of Zürich". However, the most important task of gnomes is to take care for mushrooms, toadstools and fungi. The fact that there are still zillions of these around is the proof of existence of gnomes and goblins.

The Fungi Kingdom includes a tremendous number of ecologically mighty important organisms. They break down dead organic material and continue the cycle of nutrients through the ecosystems. Most vascular plants cannot grow without the symbiotic fungi that inhabit their roots and supply essential nutrients that are otherwise not available to the plants or that they cannot produce. A beautiful example of symbiosis. Other fungi provide us with particular pharmaceutical products such as penicillin and other antibiotics, foods like mushrooms, truffles and morels, and the bubbles in our bread, champagne and beer.

Fungi are subject to a tremendous degree of diversification. The potential of chemicals that are produced by fungi is unrivalled, going from extremely beneficial β -glucans to extremely dangerous products such like α -amanitine. This is an octapeptide that occurs in Amanita phalloides. Amanite poisoning asks every year for victims, despite all the issued warnings. The first signs of the poisonous activity show up after 12-24 hours. Lethality of α -amanitine occurs after 3-10 days whereby the liver and kidneys are irreversibly damaged.

A large number of fungi are of sincere interest because of their β -glucans, polysaccharides largely made up from glucose. Agaricus subrufescens, better known as Agaricus blazei or Hime-Matsutake, is one of the most important exponents thereof. In Brazil it is known as Cogumelo de Deus (Gods mushroom). A.blazei has an extreme (water-soluble) 1,3/1,6- β -glucan content, totally outperforming yeasts that are currently used for the production of β -glucans. Many β -glucans are poorly soluble in water, and are made soluble by reaction with chloroacetic acid (CM-glucan); apart from the fact that CM-glucan is always contaminated with unreacted chloroacetic acid, the activity is minimal 200 times lower.

The polysaccharides from *A.blazei* are used to treat patients with gastric and colorectal cancer, and are extremely powerful stimulants of the immune system. There is a massive set of in vitro data available that β -glucans (e.g. arabinoxylane) have powerful anti-tumour and antiviral properties. We discussed some of this already with you in our paper "Cosmetic Chemistry of Rice" relative to MGN-3. This is a food supplement described as a hemicellulose complex containing arabinoxylane as the major component, produced upon enzymatic hydrolysis of rice bran with the enzymes from the mycelia of Shi-itake, Kawaratake and Suehirotake mushrooms. These polysaccharides bind specifically to specialised white blood cells (macrophages, granulocytes, natural killer cells), and they produce cytokines that stimulate the formation of new white blood cells. It is a true chain reaction whereby the defence mechanism is massively improved. *A.Blazei* sincerely contributes to the body-own production of interferon and interleukin, reason why it is successfully used in Japan for the treatment of various forms of cancer and hepatitis C.



Fig.1: AGARICUS BLAZEI MURRILL

In the past it was not possible to cultivate *A.blazei*. Prof.Iwaida of the reputed Tokyo University succeeded in that, enabling controlled cultivation of *A.blazei*. China and Brazil are major exporters. The number of scientific publications on *A.blazei* is quickly increasing, because it is truly one of the breakthroughs in cancer research.

The number of cosmetic products containing *A.blazei* is rather limited, although extracts are commercially made available by Campo Research and Garuda International. That is different for other mushrooms with a high level of water-soluble β -glucans such as *Ganoderma lucidum*, commonly named reishi (Japan) or ling zhi (China).

Based on the work of Komota it is concluded that red reishi is essentially non-toxic, although the fruiting body is extremely bitter. Although edible, it's not really gastronomy to eat red reishi. Black reishi (kokushi) lacks this bitterness, although the taste is also not appreciated. The bitterness comes from oxidised lanosterol species with well-known structure. Also ergosterol and 24-methylene cholesterol derivatives have been identified, and some particular sterols have been isolated specific for reishi, such as ganodesterone and ganoderic & lucideric acids. This triterpenoid fraction

has shown powerful in vitro anti-tumour activity, probably ganoderic acid being the exponent thereof. Highly significant is also the presence of hypoglycaemic polysaccharides and proteoglycans. Also these were demonstrated to exhibit in vitro anti-tumour activity. After chromatographic isolation it was shown that reishi-specific polysaccharides exhibited the strongest anti-tumour activity.



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Fig.2: RED REISHI (GANODERMA LUCIDUM)

Although the cytotoxic activity of both red and black reishi is high and beneficially applied for cancer treatment, this is cosmetically a useless parameter as EU Legislation prohibits medical claims on cosmetic products. On the other hand, strengthening of the immune system is real candy for the cosmetic chemist, as weakening of the immune system has been shown to be a major factor in the ageing process. A well-performing immune system automatically means a healthy cellular turnover and the proper tools for cell diversification, while avoiding premature apoptosis. The application of *Agaricus blazei* and *Ganoderma lucidum* in personal care & cosmetic products is a logical approach, as these are the most powerful sources known for water-soluble β -glucans, that are specific for these species of mushrooms.

We agree with you that it is not the easiest thing to do to put these unique β -glucans to work. Recently we discussed with you transdermal transport, and this is important as the activity of β -glucans is only taking place in the living skin where new cells are made and trained for their future job. Thus, the composition of the carrier system (gels, emulsions or micro-emulsions) creates already quite a bit of boundary conditions. Next, the manufacturing procedure is important to creating the vehicle to make transdermal transport effective.

Admitted, Nippon Menard are close to the source of reishi, but they have developed the technology to put these β -glucans from *Ganoderma lucidum* to work in their Embellir product line. They have superbly applied the Japanese credo “do what you’re good at”. Development of the required production techniques is important, and that is what they have done extremely successfully. The use of liquid crystalline structures obtained via high pressure emulsification enables to achieve the required transdermal transport phenomena. With this technique it is possible to largely reduce the amount of emulsifiers required to obtain a stable emulsion system, a technique that was in the 80’s already utilised by Japanese food emulsion producing compa-

nies, but never really reached Europe. It is than possible to obtain homodisperse emulsions. A simple experiment using a microscope at a magnification of 400 or 600x swiftly betrays the homodispersity of the Embellir emulsions. Combined with their unsurpassed hygienic conditions, comparable to a class 1 clean room operation, enables also to minimise the preservative loading of their products to obtain a superior, unrivalled consumer-friendly product.



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Fig.3: ONE OF PRODUCTION FACILITIES OF NIPPON MENARD

We have visited all the major production locations in Europe, but we were also allowed to take a look at the Menard production location in Nagoya. We have truly never observed the quality standards that are applied by Nippon Menard. We appreciate the approach that a superior product can only be made in a superior production facility. There is still a lot to learn from the Nippon Menard approach.

Nippon Menard is not only the superior quality company; it is also a very social company. Part of the earnings is re-invested in the Menard Museum in Komaki (see <http://www.menard.co.jp/museum/>), a museum established by the founder and his wife, Mrs./Mr.Nonogawa. Approximately 1300 paintings and other pieces of art are on permanent exhibition, including master pieces of Marc Chagall, Vincent van Gogh, Pablo Picasso, Georges Braque and a whole range of great Japanese artists (who, we have to admit it, we're not very familiar with, but they are beautiful indeed!).

Personal care & cosmetics is the industry of beauty and care: pieces of art. We have experienced that Nippon Menard are the ultimate exponent thereof, whereby there is a major role for mushrooms.