Pollen: Nutrition, Functional Properties, Health

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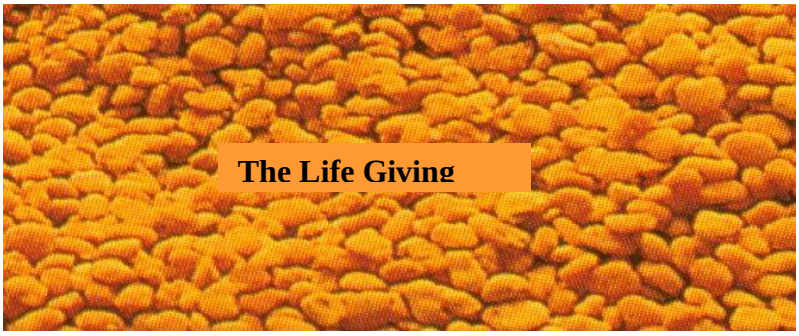
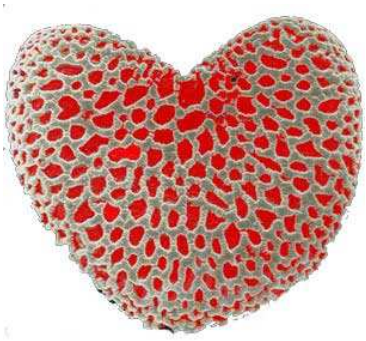




tiger lilly pollen, courtesy www.pbrc.hawaii.edu

The old Egyptians describe pollen as "a life-giving dust." Pollen and its nutritional value is still surrounded by mysteries. It is called the only perfectly complete food. The consumption of plant producing seed, the pollen, is praised in the Bible, Genesis 1:29: *And God said, See, I have given you every plant producing seed, on the face of all the earth, and every tree which has fruit producing seed: they will be for your food.*

The earliest references found to its medical uses are in books by Arab and Jewish physisicans in Islamic Spain, although pollen may not have been bee collected. Maimoides (1135-1204) a physician in Cordoba, recommended its use as an astringent and sedative tonic. In the early 1200's Ibn el-Beithar described it as aphrodiasiac, also beneficial for the stomach, giving back the fervour of the blood and curing swellings produced by eating certain foods[34].

In new times bee collected pollen began to be used for human nutrition only after the second world war, when pollen traps were developed.

In this review it will be distinguished between the effects of bee pollen and of hand collected pollen which will be named flower pollen.

COMPOSITION AND NUTRITION

Pollen Composition and nutritional requirements: main components, after [21, 25]

Main Components	g in 100 g	RDI* (g/day)
Carbohydrates (fructose, glucose, sucrose, fibers)	13 - 55	320
Crude fibers	0.3 – 20	30
Protein	10 – 40	50
Fat	1 – 13	80

As shown in chapter 1 of this book, there is a big variation of pollen composition. This variation is mainly due to the botanical origin of pollen. Thus, for some pollen types there is a better contribution of pollen to the RDI than for other pollen types. Consequently, it is important to establish the RDI coverage for the pollen types that are offered by companies or beekeepers by making a chemical analysis of the marketed pollen.

Carbohydrates

They are mainly polysaccharides like starch and cell wall material[146] .The sugars fructose, glucose and sucrose comprise about 90 % of all low molecular sugars[137]

Crude fibre

The crude fibre content varies considerably, this variation is due both to the determination method and to the botanical origin. Recent measurements are in a better agreement. A Swiss study reports it to differ between 10 and 13 g/ in different commercial pollen[14] while in pollen from France values between 9.2 and 14.4 g/100 g are reported[118] .

Protein

The protein can play an important role for covering the RDI. Only about 1/10 of the total protein comes from free amino acids. Pollen contains all essential amino acids (see table below). However, protein content depend strongly on the botanical origin of honey, while the qualitative pattern of the amino acids is similar in the different types of pollen[129]

Fat

There are considerable differences of the fat content and composition, depending on the botanical origin. The differences of fat content are due to the different botanical origin of pollen. There are mainly polar and neutral fats (mono-, di and triglycerides), as well as small amounts of fatty acids, sterines and hydrocarbons.

In one study 3 % of the total lipids are free fatty acid are reported, about half of them are the unsaturated acids oleic, linoleic (omega-6) and linolenic (omega-3) [146].

Manning reports in a review that 70 to 90 % of the lipids are composed of fatty acids, the average being around 90 %. In the same review he finds a big variation of the different fatty acids depending on the pollen type. Mostly pollen has a higher amount of unsaturated acids, but there are some exceptions, e.g. sunflower pollen. [96]

In a study of mixed pollen originating from different geographic origins that 50 to 60 % of the fatty acids were unsaturated: oleic, linoleic and mainly alpha-linoleic (about 70 % of all unsaturated acids) [147]

There is agreement that the main saturated acids are C14, C16 and C18 acids: myristic, palmitic and stearic acids, while the main non-saturated acids are C18 : oleic, linoleic and alpha-linoleic. The main acid is the alpha-linolenic acid is an omega-3 acid. The concentration of this acid in pollen in different pollen types varies widely, lying between 0.1 and 4 g /100 g [96]. The amount of the acid in pollen mixtures from different countries varies much less, the values vary between 1.7 and 4.4 g /100 g [147].

The alpha-linoleic acid is a so called omega-3 acid, has many beneficial effects in nutrition[141]. Compared to other food pollen has a higher concentration of most vegetable food. However, no official RDI has been established.

Other physiologically important compounds are the sterols and terpenes, but they are contained in minor quantities

Minor components

Minerals and trace elements

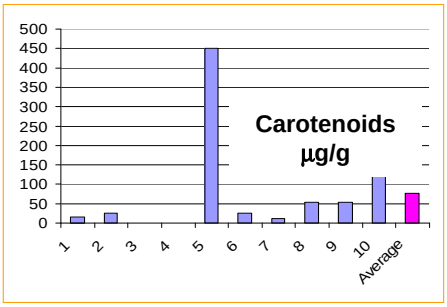
Minerals and Nutritional Requirements, after [21, 25, 102]

Minerals	mg in 100g	RDI (mg/day)
Potassium (K)	400 – 2000	2000
Phosphor (P)	80 – 600	1000
Calcium (Ca)	20 – 300	1100
Magnesium (Mg)	20 – 300	350
Zink (Zn)	3 – 25	8.5
Manganese (Mn)	2 – 11	3.5
Iron (Fe)	1.1 – 17	12.5
Copper (Cu)	0.2 – 1.6	1.2
Selenium (Se)	0.05-0.005	0.005

There is a considerable variation depending on the pollen type[146]. The main mineral is potassium. The mineral levels in pollen were also found to vary considerably in the course of the year due to differences in the floral origin of the pollen. This was true for potassium, magnesium, calcium, manganese and iron, while the zinc and copper content of pollen appeared to be more constant[62].

The sodium content of pollen is relatively low, values were found varying between 28 and 93 mg / 100 g [12, 118, 139, 145].

Vitamins and carotenoids



There is a significant nutritional contribution from most of the vitamines present in pollen: provitamine A, vitamine E (tocopherol), niacin, thiamine, folic acids and biotin. Specially in those cases, where high values have been measured, while in some pollen types the content is lower. Like other components, there is a considerable variation, depending on the pollen type.

Pollen contains significant amount of carotenoids, mainly β-carotene, are related to vitamin. But these, too depend on the botanical source of the pollen, graph for pollen collected in Brazil after[5]. (graph left)

β-carotene represents about 17 % of the totals carotenoids. French Cistus pollen contains 20 times more carotenoids than chestnut one[118].

Vitamins and Nutritional Requirements, after [21, 25, 144]

	mg in 100g	**RDI (mg/day)**
Vitamines		
Ascorbic acid (C)	7 – 56	100
β-Carotin (provitamin A)	1 – 20	0.9
Tocopherol (vitamin E)	4 – 32	13
Niacin (B3)	4 – 14.4	15
Pyridoxin (B6)	0.2 – 0.7	1.4
Thiamin (B1)	0.6 – 1.3	1.1
Riboflavin (B2)	0.6 – 2.6	1.3
Pantothenic acid	0.5 – 2	6
Folic acid	0.3 – 1	0.4
Biotin (H)	0.05 – 0.07	0.045

Compared to the vitamin-richest corns, fruits and vegetables, pollen has 20 times more vitamine A and significantly more panthothenic and folic acids and biotin.

Unconjugated vitamin D and its metabolites were investigated in the pollen of *Pinus nigra Ar.* and *Pinus sylvestris L.* It was found that vitamin D (D2, D3) was present in the pollen in amounts about 2 micrograms/10 g and 25-OHD3, 24,25-dihydroxycholecalciferol [24,25-(OH)2D3] and 1,25-dihydroxycholecalciferol [1,25-(OH)2D3] between 0.1 and 3 micrograms/10 g of pollen, dependent on pollen species and method[133]
Coenzym Q was detected in pollen from China in quantities from 0 to 193 mg/kg [170]. The recommended daily intake of food supllements with Coenzym Q is about 50 to 100 mg daily.

Variation of pollen nutritional composition of several pollen gather in France after[118]
values per 100 g

	RDI	Cistus	Chestnut	Willow	Heather	Poppy	Rape
Calories	2000 - 2500	354	316	354	319	316	334
Proteins. G	50	14.2	19.56	15.5	15.5	22.8	22.85
Lipids		6.56	4.19	5.8	3.26	3.26	8.79
Linoleic acids g	8	0.7	0.31	0.31	0.13	0.31	
Alphalinoleic acid g	1.6	0.52	0.15	0.33	0.55	0.55	
Polyunsaturated acids %		57.65	54.30	49.50	49.50	68.90	
Carbohydrates g		58.03	52.17	46.77	64.5 g	48.66	40.97
Fibres g	25 g	12.80	14.4	14.4	13.0	9.2	13.1 g
Vitamins, mg							
Vitamin B1	1.4	0.80	0.52	1.01	0.38	0.47	0.67
Vitamin B2	1.6	0.76	1.17	0.86	0.86	0.36	0.86
Vitamine B3	18	4.60	6.7	7.1	4.79g	2.27	0.37
Vitamine B5	6	0.86	1.24	0.9	0.9	1.45	0.75
Vitamine B6	2	0.27	0.29	0.30	0.25	0.04	0.44
Vitamine B9	200	124	371	844	128	157	199
Vitamine C	60	14.2	14.3	29.8	20.2	67.1	11.11
Vitamine E	10	27.8	4.2	11.8	9.28	1.44	0.69
Minerals, mg							
Copper, Cu	2.5	0.68	0.61	0.85	0.63	0.63	
Magnesium, Mg	300	26.5	50.1	71.4	60.1	41.3	
Phosphor, P	800	200.1	337.5	566	279.9	448	
Zinc, Zn	15	2.26	6.47	4.7	3.2	4.41	
Potassium, K	8000	370	504	484	433	433	
Sodium, Na	2000	26	31	31	31	24	
Polyphenols mg		1033	1959	2086	1500	1788	1420
ORAC. mmoles/g		151	536	406	199	379	283
Flavonoids. Mg							
Kaempferol-3.0- glucos.		72.6	61.9	575	48.3	648.3	
Isorhamnetine-3.0- glucos.		22.5	282	158	7.1	37.1	
Rutine		149.7	ND	335	1207	239	
Luteoline-7-glucoside		7.6	13.9	6.6	30.7	175	
Phytosterols mg		276	232	191	NA	NA	
Ess. Amino acids. mg							
Threonine	390	680	640	670	930	680	
Valine	700	870	840	790	130	1130	
Methionine	910	20	420	420	660	590	590
Isoleucine	700	690	660	640	950	950	
Leucine	980	220	1130	1130	1130	1575	
Phenylalanine	980	700	660	770	940	700	
Lysine	840	130	1080	1020	1020	1465	
Tryptophane	245	160	160	160	170	273	160
Totals	5845	5870	5590	5710	5710	7924	
Cystine		160	330	170	330	170	360

NA – not analysed

Flavonoids

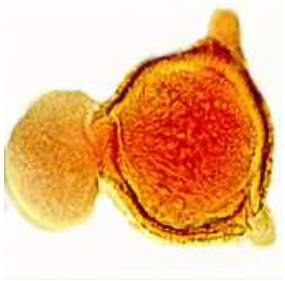
These are the main secondary compounds of pollen. They are responsible for the colour of pollen and are either colourless or yellow, red and purple[146]. The flavonoids are also responsible for the bitter taste of pollen. Most flavonoids exist as glycosides, called aglycones, i.e. sugar derivatives. In one study their amount varied between 1293 and 8243 mg/100 g, in another, between 530 and 3258 mg/100 g [24, 88] the variation been due to variation of the flavonoid content of the different pollen types. Rutin seems to be the main flavonoid[138]. There are no official daily allowances for flavonoids, suggestions lie between 200 to 1000 mg a day.

Sterols and terpenes

Pollen contains also 0.1 – 0.4 % sterols, some of which having various biological properties like β-estradiol, β-sistosterol, stigmasterol and fucosterol, as well as 0.1 to 0.2 % mono-terpenes [146].

Cistus pollen contains mostly delta-5-avenasterol (108 mg/100 g) and 24- thylcholesterol (76 mg/100 g), chestnut pollen mostly betasitosterol (111 mg/100 g) and brassicasterol (46,5 mg/100 g); willow pollen: betasitosterol (74 mg/100g) and delta 5- avenasterol (39 mg/100 g) [119].

Pollen digestion and pharmacodynamics



Doubts have been raised, whether the tough shell of pollen can be cracked and digested by humans. It has been found out, that in animal experiments pollen does longer contain their content when they have left the digestion tract. This conducted to the hypothesis that the nutritional content of pollen can be released by the digestive juices in animals [129, 136]. There is evidence that pollen can be persorbed (direct absorption of pollen grains into the blood stream) in the digestive tract of dogs, rabbits and humans [70]. In in-vitro simulation of human digestion pollen was partly digested [50], where as there were differences in the degree of digestion of poppy and hazelnut pollen, with an average degree of digestibility of 15 % for carbohydrates and 53 % for proteins. In this case has been hypothesized that pollen is insufficiently digested and that cracking will improve the digestibility and bioavailability [128].

Combination of protamex hydrolysis and ultrasonication can degrade the pollen coat and entirely disrupt both the exine and the intine of the pollen[37]

Different companies offer cracked bee pollen, claiming that this product is better digested. On the other hand, there are many studies in humans with whole bee pollen (see next section) showing that a part of the bee pollen content is digested and is bioavailable. However maceration of pollen for several hours in water or other liquids is recommended in order to improve digestibility, a method used also for other heavy digestible grain products.

Bee pollen extraction improves the antioxidant activity, best extraction is achieved with ethanol. Extraction with water alone yields also extracts with higher antioxidant activity than that of whole pollen[85]. Also Remy Chauvin carried many of his rat nutrition experiments after maceration of pollen with water for several hours and subsequent filtration, that means without the water insoluble pollen (see below). In the book on pollen by the Ukranian pharmacist Tikhonov and his team many active pollen preparation were also made from the water soluble supernatant after pollen maceration with water (see further down **Ukranian pollen preparations against different diseases).** Thus it seams that many of the bioactive substances of pollen are easily released from the pollen.

After pollen has reached the human digestive tract the pollen grain begins to swell. Do to the uptake of water they increase in size and are enzymatically activated. The material, contained in pollen wall break up and materials (enzymes and allergens) leak out. This leads to structures similar to the pollen tube[94]

The exines of the pollen corn cannot be decomposed in the gastrointestinal tract as very few animals and microorganisms are enzymatically capable of disintegrating the highly resistant sporopollenin which makes up the pollen grain wall. Thus, only the pollen content in the submicroscopic area of the pollen wall can be utilized as foodstuff[94]

Pollen in animal nutrition

Chauvin carried out animal feeding experiments with pollen. He fed different types of pollen and compared the weight gain of pollen fed mice in comparison with the controls, fed with casein[29]:

Effects of pollen feeding on the weight increase of mice, after[29]

	Gains in gram							
	First week		Second week		Third week		Total, Sign. *, **	
	P Extract	Whole P	P Extract	Whole P	P Extract	Whole P	P Extract	Whole P
Rape	6.0	5.1	5.1	6.5	5.4	3.1	16.4 *	14.7 *
Clover	5.7	5.3	5.2	6.3	5.4	2.1	16.3 *	13.8 *
Sweet chestnut	6.4	3.7	4.5	7.4	4.7	2.5	15.6 **	13.5 **
Mixed pollen	7.7	4.3	5.4	7.4	5.5	2.6	18.7 *	13.3 **
Control (casein)	3.9	5.4	4.4	4.6	5.9	2.7		

* - Significant or non-significant according to Students t-test.

Whole pollen and aqueous extracts of pollen were fed to mice, together with the mice feeding with casein, in a proportion of 50% pollen of the total feeding. The aqueous pollen was prepared by maceration of pollen in water

for several hours and subsequent filtration. The filtrate was boiled and the resulting precipitate was fed to the mice. Feeding of casein with less than 10 % of pollen did not produce a significant effect. At the end of the experiment it was found, that the mice which had pollen in their diet had eaten less food, meaning that pollen improved the food utilisation.

In another experiments Chauvin found following increases in % of the initial weight, mice being fed with natural pollen added to a casein food, being 50 % of the total food[28]:

Fruit pollen: 46 %; Sweet chestnut pollen: 44 %; Poppy: 43 %; dandelion: 37 %; Rockrose:36 %; Maize: 36 %

Heather: 34 %; Clover: 16 %.

In addition, Chauvin found out that mice can be successfully fed on pollen only. However, the weight increase of the males was much slower than that of the she-males.

In another study the ingestion of bee pollen by rats reveals that it improves the maternal nutrition of rats without affecting the normal fetal development and thus might be a favourable nutrient during pregnancy. However the hyperglycaemic effect revealed in the preceding assay can not be underestimated [169]

Mice feed with bee pollen from different plants for 6 months show an increase of the reproduction rates [142].

Feeding with 200 mg/kg pollen to New Zealand white rabbits increased body weight of does, conception rate, milk yield, litter size; improved biochemical profiles of blood, and also kit growth and their survival rate until weaning[8].

Feeding of casein containing 5 % of pollen let to a total weight increase of poultry of 4 kg, while the controls increased by 2.7 kg (initial weight was 5.8 kg). In other experiments addition of 5 % of pollen to the feeding of laying hens resulted in a better survival rates, which was even better than when 10 % pollen were fed [151]

It has been shown that fed chickens with bee pollen leads to a better development of the small intestine villi from the duodenum, jejunum and ileum. These findings suggest that bee pollen could promote the early development of the digestive system [161].

Bee pollen product supplementation to horses in training seems to improve feed intake

The objective of this study was to determine the efficacy of supplementation of Dynamic Trio 50/50, a bee pollen-based product, to improve physical fitness, blood leukocyte profiles, and nutritional variables in exercised horses. No treatment differences existed for different performance parameters, while there was a trend for lymphocyte counts to be lower in BP than the controls (placebo) on day 42. Dynamic Trio 50/50 supplementation may have a positive effect on performance by helping horses in training meet their potentially increased nutrient demands by increasing feed intake and thus nutrient retention[155].

Pollen for increase of sport performance

In early days there were claims that bee pollen is an optimal food for sportsmen. Indeed, competitive sportsmen in some countries have used bee pollen preparations or extracts as a dietary supplement in the belief that it can lead to an improvement in performance. Controlled experiments with swimmers indicate that no positive benefit was obtained from the use of this supplementation. However, the number of training days missed due to upper respiratory tract infections was much less in the bee pollen treatment group (4 days) than in the placebo group (27 days). In a study of longer duration, this difference could lead to an improved performance by the bee pollen treatment group due to fewer interruptions in training [99]. On the other hand, another test with long distance runners showed that neither pollen nor protein supplementation improved the performance or the blood haemoglobin values in comparison with the controls (placebo)[166].

Experiments with sportsmen in Russia, reviewed by Asavova et al. [7] discusses different studies in Russia

1. Ivashkiavicene, 1977 tested the intake of twice a day intake of 10 g pollen on the performance on the national light athletic team of Lithuania. The performances increased, together with an increase of the blood haemoglobin values. Analogous positive experiments were carried out with basketball and handball professional players.
2. Vassilecksy and Maltsev, 1988 tested the pollen intake on the performance of military trainings. They added to the daily ration of 50 g pollen before lunch. In the recovery period between the marches the men took 70 g of pollen. The control group did not take pollen. A number of physical parameters were measured: weight, pulse, the spirometric value, as well as performance and psychological tests. The authors concluded that pollen

can be successfully used for recovery after physical strain periods, improving also the psycho-vegetative condition.

3. There were successful performance tests with honey/pollen mixtures (50 g of honey with 20 to 40 g pollen)
4. The dosage of pollen was different varying between 20 and 50 g daily.

Nechaeva tested intake of twice a day of two teaspoons pollen (10 g) for 15 days and tested the performance of Russian sport female students. Following tests were carried out: measurement of body mass, performance of Stange's breath holding test, measurement of the viso-motoric reaction, hanging on the bars, 30 m runs with maximal speed, measurement of heart rate afterwards, then a 5 minute step test with a step height of 30 cm, 30 climbs per minute followed by a 5 minute rest. There was a significant increase of the reaction of the organism to hypoxia, as measured by the Stange test by 19 % , and an improvement of the viso-motoric reaction[112].

Generally, organism stress and increased sport exercises lead to a decrease of the immune reaction. This leads to increase infection risk of sportsmen. A Russian study states that the immune reaction measured by the reactivity of T lymphocytes of sportsmen normalised after the intake of pollen in honey within 8 weeks[1]. In another Russian study it was found that pollen intake by sportsmen in swimming and cross-country skying leads to increased values of the haemoglobin and protein values[124].

FUNCTIONAL PROPERTIES

Parts of this section have appeared in[21]

The main biological components of bee pollen are the phenolic acid derivatives and polyphenolic compounds, mostly flavonoid glycosides. The flavonoids are so called secondary plant compounds which have different important physiological and pharmacological activities. They possess diverse biological properties such as antioxidant, antiaging, anticarcinogen, antiinflammatory, antiatherosclerosis, cardioprotective and improve the endothelial function. Most of these biological actions have been attributed to their intrinsic reducing capabilities. They may also offer indirect protection by activating endogenous defensive systems and by modulating different physiological processes [59].

Another group of compounds contained in pollen are the phytosterols. Among several bioactivities the most prominent is their blood cholesterol-lowering effect via partial inhibition of intestinal cholesterol absorption. Other claimed benefits of phytosterols are possible antiatherogenic effects as well as, immune stimulating and antiinflammatory activities carried out mainly by beta-sitosterol. Furthermore, there is emerging evidence suggesting that particularly plant sterols may have beneficial effects against the development of different types of cancers, like colorectal, breast and prostate cancers. It is not clear whether mechanisms other than the established cholesterol-lowering action of phytosterols could also contribute to these potential health benefits [154].

Functional properties of pollen in cell and animal studies (see references in the text)

Effect	Tested pollen type
Antibacterial and antifungal	Bee pollen
Antioxidant	Bee pollen
Radiation- protective and hepatoprotective	Bee pollen
Chemopreventive and antitumor	Bee pollen, flower pollen
Anti-inflammatory	Bee pollen, flower pollen
Anti-osteporosis	Bee pollen
Anti-diarroe	Bee pollen
immunomodulating	Bee pollen
Probiotic and prebeiotic	Bee pollen
Antiaging	Bee pollen,
Antiatherogenic	Bee pollen, flower pollen
Positive influence on the urinary bladder of mice	flower pollen
Anti-depressant	Bee pollen
Cardioprotective	Bee pollen

Antimicrobial activity

After isolation of different flavonoids from *Eucalyptus globulus*, *Ranunculus sardous* and *Ulex europeans* bee pollen it was concluded that the herbacetin derivates from *Ranunculus sardous* and *Ulex Europeans* had a marked antibiotic activity against *Pseudomonas aeruginosa*. On the other hand, *Eucalyptus globulus*, mainly rich in quercetin derivates, did not show any antibacterial activity [20].

In other study it was found that bee pollen hydrophobic compounds with unknown nature had antibacterial activity against *Viridans streptococci* [150].

Antibacterial activity of Turkish bee pollen was studied against 13 different bacterial species pathogens for plants (*Agrobacterium tumefaciens, A. vitis, Clavibacter michiganensis subsp. michiganensis, Erwinia amylovora, E. carotovora pv. carotovora, Pseudomonas corrugata, P. savastanoi pv. savastanoi, P. syringae pv. phaseolicola, P. syringae pv. syringae, P. syringae pv. tomato, Ralstonia solanacearum, Xanthomonas campestris pv. campestris and X. axonopodis pv. vesicatoria*). The results showed that the Turkish bee pollen extract have an inhibitory effect against all pathogens. The conclusion of the study shows that this bee-pollen extract has a potential to became a seed protectant because some of the bacterial pathogens are transmitted through the seeds[11].

On the other hand the assays carried out with Turkish bee pollen methanol extracts at concentrations from 0.02 % to 2.5 % had no inhibition activity against different spoilage and pathogenic microorganisms [47].

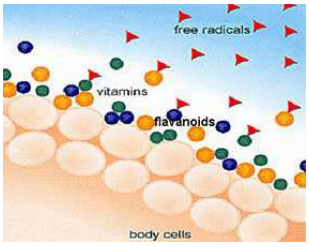
Pollen bread was found to possess an antibacterial activity against *Staph. aureus* and *S. epidermidis* [9].

In a recent study with 80 % ethanol extracts of Brazilian bee pollen antibacterial activity was exibited against *Staphylococcus aureus, Bacillus subtilis*, *Pseudomonas aeruginosa* and *Klebsiella sp* [26].

The antibacterial substances of bee pollen, active against *Streptococcus viridans* are similar to the ones found in propolis and honey combs[150].

Pollen has also significant **antifungal** activity against different pathogens[81, 114, 115]

Antioxidant effects



Oxidative stress is thought to contribute to the development of chronic and degenerative diseases such as cancer, autoimmune disorders, aging, cataract, rheumatoid arthritis, cardiovascular and neurodegenerative diseases [120]. An antioxidant is a molecule capable of slowing or preventing the oxidation of other molecules and so to prevent such changes.

In several studies a close relationship between pollen antioxidant bioactivity and phenolic compounds has been reported [23, 24, 87, 88]. However the correlation between these two parameters is not that clear[97]. It was also found that the bee pollen antioxidant activity is pollen species-specific [4, 49, 87, 88, 97] and independent of its geographical origin [4].

The difference between the antioxidant activities of the different pollen types harvested in Romania is about 10 fold. The antioxidant activity of Pinus and Knautia pollen is relatively low while that of Matricaria and Salix pollen is higher[97].

The values vary from: FRAP values, mM Fe^{2+} /g 0.25 to 5.35; DPPH in Trilox equiv. mM Trilox/ g: 0.27 – 2.8. In comparison: for most vegetables and fruits the same values are about a factor of 200 to 1000 times smaller[116].

Bee bread was also found to have a high antioxidant activity [10, 108].

The antioxidant abilities of *Cistus ladeniferus* pollen extracts were evaluated using lipid peroxidation model system. Ethanol-soluble fraction (ESF) was most active followed by hot-water fraction (HWF). These abilities of pollen extracts were higher than that of 5 mM ascorbic acid and were similar to that of 1 mM α-tocopherol. Superoxide-scavenging capacities were decreased in the order water-soluble fraction > HWF > ESF. ESF showed the highest hydroxyl radical scavenging ability among these samples. The pollen extracts showed DPPH radical scavenging ability. Particularly the ability of ESF gradually increased with passage of the time (about 80% to 10 min)[106].

The antioxidant status, estrogenic/anti-estrogenic activity and gene expression profile were studied in mice fed with *Cystus incanus L.* (Cistaceae) reach bee pollen from Croatia. The pollen modulated antioxidant enzymes (AOE) in the mice liver, brain and lysate of erythrocytes and reduced hepatic lipid peroxidation (LPO). Bee pollen induced

25% of anti-estrogenic properties while no estrogenic activity was found. Differential gene expression profile analyses after bee pollen enriched diet identify underexpressed gene Hspa9a, Tnfsf6 (liver) and down-regulated gene expression of Casp 1 and Ccl21c (brain) which are important in the apoptosis pathway and chemotaxis [135]

The free radical scavenging ability decreases with the storage of dried bee-pollen at room temperature and can loose about 50 % of the antioxidant power within 1 year [24].

Experiments with feeding rats were conducted with bee pollen during one month studying the state of the erythrocyte redox system. It was established that the content of glutathione, total SH-groups as well as the activities the antioxidant enzymes glutathione peroxidase and glutathione reductase were increased in comparison with the control group [41].

Anti-radiation and hepatoprotective effects

Anti-radiation

The free radical scavenging activity prevents irradiation damages by free radicals. This means that an antiradiation effect of pollen should be expected [120]. Indeed, it was established that small x-irradiation doses activate the lipid peroxidation and antioxidant system enzymes in mice liver. The introduction of a bee pollen extract to the diet of the animals normalized the activity of several glutathione system enzymes in mice liver [13].

Application of beta-carotene oil or bee-pollen both abolished radiation effects but did not influence the effects caused by chemical toxics. The authors supposed that the selective action of the observed drugs is connected with the antioxidant activity of pollen and beta-carotene [6].

Hepatoprotection

The effect of bee pollen on liver functions in old rats was studied. After one month they had a diminution of malondyaldehyde levels and the sulphydryl groups (SH-G) content was normalized. Also serum urea and protein levels were significantly improved at the end of the experiments [158].

Bee pollen extracts were administered to rats, intoxicated by carbaryl. Levels/activities of total protein, albumin, glucose, triglyceride, T-cholesterol, T-bilirubin, blood urea nitrogen, creatinine, uric acid, magnesium, sodium, potassium, chloride as well as different liver enzymes were evaluated in the serum samples of the treated rats in comparison to the controls, showed a detoxification effect of bee pollen. While carbaryl caused negative changes in most of the oxidative stress markers and of the serum biochemical parameters investigated in the controls, these effects were relieved with the administration of bee pollen [45]

It was recently found that feeding mice with bee pollen protects from the toxic effects of the pesticide protoxur, a very toxic pesticide, which is thought to induce oxidative stress [46].

Paracetamol intoxicated rats fed bee pollen extract preparations, Cernilton and Cerniltin showed that Cernilton increased the survival of the rats by preventing hepatic lesions. It has been hypothesized that this action is effective and not prophylactic [71].

Enzymatic hydrolysates from bee pollen of *Cistus ladaniferus* prepared by six proteases and angiotensin I - converting enzyme (ACE) inhibitory activities were investigated. These results suggest that there is a very high antioxidant and ACE inhibitory activities in hydrolysates from bee pollen of *Cistus ladaniferus* [107] .

Bee pollen of *Eucalyptus glob.* and *Salix. atr*. showed antidiarietic activity in rats[19]

Cardus [35] and castanea[175] bee pollen was shown to have a hepatoprotecting effect in mice and rats These positive effects were confirmed in humans. Administration of pollen bread to patients suffering from chronic hepatitis showed that after 30 days their clinical situation improved measured by the albumin/globulin proportion in plasma and the microscopic structure of liver [65]. These effects could be explained by the pollen induced activation of the antioxidant system liver enzymes and the decrease of lipid peroxidation [13].

Chemopreventive and anticancer activity

The pollen flavonoids quercetin, rutin and chyrisin have been shown to have a chemopreventive activity by increasing apoptosis (programmed cell death), thus acting in cancer prevention[77, 121].

Bee pollen

The morphological changes in aged canine benign prostatic hyperplasia were followed after bee pollen treatment, 5-10 g/kg administered in oral doses for 2 months to aged dogs with prostatic hyperplasia. Prostate size was

reduced both at one month and at 2 months. Microscopic examination showed marked diminution in gland diameter, epithelial cell heights and less papillary infolding of the epithelia compared to untreated controls. No effect on plasma estradiol or testosterone levels was observed and no toxicities were reported [93].

A chloroform extract of Brassica bee pollen showed anticancer activity by increasing apoptosis of human prostate cancer PC-3 cells[168].

The estrogenic/antiestrogenic activity and the genotoxicity/antigenotoxicity of bee pollen from Salix alba L and Cystus incanus L and its derivative extracts in yeast and human cells was investigated. All samples showed a marked inhibitory effect on the activity of the natural estrogen 17 beta-estradiol (higher than 90% for extracts 2) and failed to cause estrogenic activity and chromosome damage. At least one preparation from each species showed a marked antigenotoxic effect against the action of the anticancer drugs mytomicin C. bleomycin, and vincristine. Bee pollens from C. incanus and S. alba were found to be neither genotoxic nor estrogenic as well as effective estrogen inhibitors, and able to reduce the chromosome damage induced by the three cancer drugs used, thus supporting their use as a safe food supplement and future chemoprotective/chemopreventive agents[122].

Extracts of Turkish bee pollen inhibited respiratory burst of K-562 cancer cells[3].

Bee pollen extracts inhibited the proliferation of human umbilical vein endothelial cells, but to a slighter extent than Chinese red propolis[68]

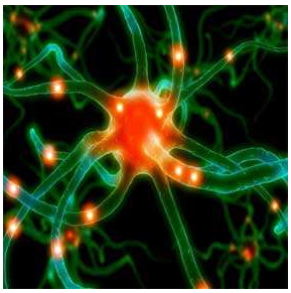
Bee pollen polysaccharides from *Rosa rugosa* (WRPP) were extracted and fractionated. All the fractions had significant anti-proliferative activity in HT-29 and HCT116 cells; the neutral and acidic fractions were shown to have significant synergistic effects which accounted for the antitumor activity of bee pollen polysaccharides from *Rosa rugosa* in vitro[160]

Flower pollen

Nine human-derived cancer and non-cancer continuous cell lines were employed to evaluate the relative in vitro activity of the pollen extract, Cernitin T-60. Responses of the cell lines to the drug were assessed by measuring growth and cell survival as determined by cell count. The results demonstrated that of the 9 continuous cell lines tested, only those derived from the human prostate were growth inhibited by the pollen extract, whereas the non-prostate derived cells exhibited variable degrees of resistance to the T-60[56]. Another experiments with Cernithin extract showed that it had an anti-tumour activity of mice with lung cancer[52]

2,4-dihydroxy-2*H*-1,4-benzoxazin-3(4*H*)-one (DIBOA), a cyclic hydroxamic acid isolated from had collected rye pollen, has a strong inhibitory effect on the growth of prostate cell lines[178].

Antiinflammatory activity



Inflammation is a physiological response to the damage of tissues or cells that is caused by physical or biological agents and also free radicals involving different reactions intended to remove the cause and repair the damage.

The antinociceptive and antinflammatory activity of pine (*Pinus densiflora*) flower pollen extracts (100 and 200 mg/kg) in mice were tested. The positive results of pollen on acid acetic- induced writhing, on formalin-induced paw licking and on the hot plate test suggest that the analgesic effect may be related to the antinflammatory, neurogenic and narcotic properties of pollen. Positive results in carragenan-induced paw oedema and arachidonic acid-induced ear oedema suggest that *Pinus densiflora* pollen extract acts on cycloxygenase and lypoxygenase activities [30].

The anti-inflammatory effect of ethanol extract of Cistus bee pollen of Spanish origin was tested on rats. The results show a potent anti-inflammatory activity by the inhibition of NO production, besides the inhibitory activity of COX-2. Some flavonoids included in bee pollen may partly participate in some of the anti-inflammatory action[98]

Different health enhancing effects in animal and cell experiments

Anti-osteoporosis effects

Osteoporosis is defined as a reduction in bone mass and disruption of bone architecture resulting in reduced bone strength and increased fracture risk.

Bee pollen water-solubilized extract from *Cistus ladaniferus* has an inhibitory effect on bone resorption in rats femoral tissues and osteoclastic cell formation in bone marrow cell culture *in vitro*. Thus bee pollen extract has stimulatory effects on bone formation *in vitro* [58]. The active factor of this effect, a bee pollen protein, has been characterised [57].

It was shown by the same research group that water-solubilized extract from *Cistus ladaniferus* pollen causes a significant increase of alkaline phosphatase, an enzyme that participates in bone mineralization. The oral administration of the water-solubilized bee pollen extract from *Cistus ladaniferus* to rats caused a significant increase in calcium content, alkaline phosphatase activity and DNA content in the femoral-diaphyseal and metaphyseal tissues, indicating that the extract exerts anabolic effects on bone components *in vivo* [172].

The water-solubilized extract from *Cistus ladaniferus* bee pollen has a preventive effect on bone loss in STZ-diabetic rats, and also a restorative effect on serum biochemical factors in diabetic rats [173].

Primary and secondary humoral immune response (the level of specific IgM and IgG) as well as the intensity of delayed-type hypersensitivity to sheep erythrocytes were investigate in rabbits fed with bee pollen load for a month. It is shown that bee pollen is an immunomodulator. It stimulated humoral immune response and changed the reaction of delayed-type hypersensibility [40].

Anaemia

Anaemia is characterized by a low number of red blood cells. The effects of 10 g/kg/day of oral bee pollen on haemolytic anaemia animals were studied on the hemopoietic system of mice and rats. The results showed that bee pollen markedly antagonized the inhibition of the hemopoietic system and reduced white blood cells in these animals [162]. Intake of bee pollen by rats induce a significant increase of the red blood cells [28].

Similar studies in healthy rats and rats with nutritional ferropenic anaemia were carried out, examining the effect of the addition of 10 g/kg/day of multifloral bee pollen on a standard diet. The bee pollen group showed a better weight gain, an increase in the haemoglobin levels and a decrease in platelets. Platelet concentration constitutes a haematic parameter that reflects the state of the iron within an organism. It was concluded that bee pollen improves the digestive absorption of iron [61].

Other effects

Bee Pollen

Antidiarroe activity

Pollen extracts from bee collected *Eucaliptus globulus* labill and *Salix atrocinerea* Brot were tested on Swiss OFFI mice. The results showed that both bee pollen species have antidiarrhoeal activity. However, they have some differences, *Eucaliptus globulus* Labill. Bee pollen extract was more effective on retarding the diarrhoea, where *Salix atrocinerea* had a better effect in reducing the percentage of diarrhoeal excrements, but both floral types reduced the diarrhoeal excrements by 30%. This study concluded that the antidiarrhoeal activity, of the studied bee-pollen, may be due to polyphenolic compounds, especially quercetin, although some others compounds could have a role on this activity and may be responsible for the differences on the results [19].

Immunomodulator

Bee pollen is an immunomodulator, stimulating humoral immune response and changed the reaction of delayed-type hypersensitivity in rabbits[40]. In a Chinese study in mice it was shown that ethanol and acetone extracts, as well as whole Brassica bee pollen has an immunoactivating activity[125, 126].

In a study with bee pollen from Brazil it was found that supplementation of broilers food with up to 1.5 % BP resulted in increase of the bird immunity[36]

Probiotic

Recently a probiotic effect of fresh (deep frozen pollen) but not of dry pollen was announced. The probiotic lactic bacteria were not found in dry pollen, because they are not viable[118, 119].

Prebiotic

Bee pollen ethanol extract supplementation in broiler chicken significantly increases the number of Lactobacillus spp. and Enterococcus spp. in the caecum of chickens. Bee pollen could be therefore used as a potential feed additive with prebiotic activity to the poultry diet[72]

Antiaging

The effect of bee pollen on intercellular lipofuscin in mice was studied by morphological observations. The results demonstrate a reduction of lipofuscin in cardiac muscle, liver, brain and adrenal glands following administration of bee pollen. This action may be related with the anti-ageing effect of bee pollen [95].

Pollen and the heart

Feeding of polysaccharides isolated from Chinese bee pollen to rats resulted in a decrease of triglycerides, but not of total cholesterol and HDL-C[177]

The beneficial effects of bee pollen on the cardiovascular system are connected with the presence of essential unsaturated fatty acids, vitamin E, phytosterols, phospholipids and flavonoids[131]

A significant effect of bee pollen hydrolysates on an enzyme converting angiotensin I to angiotensin II (ACE), has been demonstrated. The results indicate a high antioxidative potential of bee pollen—manifesting itself by the inhibition of ACE activity—which results in hypotensive effects. Also an antiatherosclerotic effects of bee pollen has been reported[131]

Anti-depressant

Bee pollen inhibits the MAO enzyme, MAO inhibitors are generally used as anti-depressants[176]

Regulator of ovary function

Bee pollen was shown to be a potent regulator of rat ovarian functions: increase of progesterone and estradiol secretion, decrease of the Insuline-like growth factor, and increase of apoptosis[82]

Flower pollen

Cernitin (a grass pollen preparation) has different beneficial properties: lowering serum lipid levels [134, 164] reducing atherosclerosis plaque intensity [165] and decreasing platelet aggregation both *in vitro* [84] and *in vivo*[164]. These assays have been confirmed in humans[163].

Cernitin intake influenced positively the activity of urinary bladder of rats and mice [109, 111].

POLLEN IN MEDICINE

Some parts of the following section have appeared in[21]

Most applications of pollen in modern medicine are pollen preparations of flower pollen. The main reason is that only the utilization of specific pollen can guarantee a constant concentration of the active ingredients.

Benign prostatic hyperplasia

The most important use of pollen in medicine is its prophylactic and curative activity in prostate disorders. Prostatitis, or prostate inflammation, can cause difficult or painful urination that is often accompanied by a burning sensation, by a strong and frequent urge to urinate, that often results in only small amounts of urine, and by pain in the lower back or abdomen. Benign prostatic hyperplasia (BPH) is an enlarged prostate, benign meaning non-cancerous and hyperplasia, excessive growth of the tissue. BPH is the result of small non-cancerous growths inside the prostate. Chronic prostatitis is very common in elderly men, which might be related to age and hormone changes. As conventional therapies such as antibiotics are not efficient, it is not surprising that patients have turned with increasing frequency to phytotherapy and other complementary treatments, including the intake of pollen. Indeed, most of the studies reported in this section have been carried out with different flower pollen preparations, but there are also some positive results with bee pollen.

Flower pollen preparations

Most clinical tests were conducted with different flower pollen preparations: Cernilton, Cernitol and Prostat/Poltit are preparations of hand collected grass or rye pollen while Cernitin and Graminex contain different flower pollens.

In the Bruneton's Compendium of Pharmacognosy" it was mentioned that in certain countries an extract of flower pollen from a selected flora in the South of Sweden was commercialized for prostatitis treatment. The active extract includes two fractions, one is water-soluble and the other soluble in acetone rich in sterols. The hydrosoluble fraction was analysed and inhibits *in vitro* tumoral and normal prostatic cells to grow. The total extract decreases the prostate hypertrophy in rats, but given to humans no change was verified in blood levels of LH, FSH, testosterone or dihydro-testosterone. In patients with prostatic adenoma the improvement was in nycturie, important decreases in the residue post-urinate and in the long term treatment of this condition, a decrease of the prostate antero-posterior diameter was seen. The urinary debit did not suffer any changes. The effect on the other symptoms usual in the hypertrophic benign of prostate was not of statistical significance [15].

A hydroxamic acid with anti-cancer in-vitro activity[178], is probably the active compound in the flower pollen extract Cernitin which might be responsible for the symptomatic relief in patients with benign prostate hyperplasia. Seventy nine patients, ages ranged from 62 to 89 years, with this disease were treated with pollen extract, resulting in a mild beneficial effect on prostate volume and urination [174].

The pollen extract Prostat/Poltit (produced by Allergon) shows in a double blind placebo controlled study an improved symptomatic relief in man with chronic nonbacterial prostatitis/chronic pelvic pain syndrome (CNBP/CPPS). After 6 months the patients treated with Prostat/Poltit (3 tablets/day eq. 222 mg of pollen extract/day) showed a significantly lower pain score, less of voiding symptoms, less urine storage symptoms and better sexual function than the patients who had received placebo. No adverse effects were reported [44].

An overview on the promising pharmacologic agents in complementary medicine for their use in benign prostatic hyperplasia and prostate cancer agents, showed that Cernilton (the cited rye pollen extract) is one of them, besides *Glycine max* (soy), PC-SPES (a mixture of 8 herbs) and *Prunus africana (Pygeum africanum;* Tadenan) [149].

Cernitron was also tested in a study with 15 patients with chronic prostatitis and prostadynia. In 13 of the patients there was either complete or lasting relief, 2 patients failed to respond [17]. Another double blind study showed a significant improvement of the Cernitron treated patients in comparison to the controls [16]. 90 patients were treated with the same product and were divided into two groups, with and without complicating factors. Those without such factors (n=72) 78 % improved significantly. In the other group (n=18) only 1 patient showed a positive response. Cernitron was well tolerated by 97 % of the patients [130].

A clinical assay with Cernitron with a total of 89 patients with benign prostatic hyperplasia (BPH) that were treated pharmacologically for 4 months: 51 received Cernilton and 38 Tadenan (controls). Significant subjective improvement was found in 78% of the patients in the Cernilton group compared to only 55% of the Tadenan-treated patients. In the Cernilton-treated patients a significant improvement in the uroflow rate, decrease in residual urine and in prostate volume were found. This study shows that Cernilton is an effective therapy for patients with BPH [43].

The effect of the flower pollen on PPH was reviewed in 2003. 13 clinical trials were reviewed, mostly conducted with Cernilton, indicating that flower pollen therapy is a safe and effective therapy for the management of mild to moderate Lower Urinary Tract Symptoms (LUTS). The studies showed a consistent reduction in subjective symptoms and overall effectiveness ratings of 75% and greater[27]. This study is published in www.graminex.com

Bee pollen

A double-blind, placebo-controlled clinical trial was performed to investigate the efficacy and safety of 12-week intake of a bee pollen (mainly Citrus) ethanol extract (PE) supplemented food in 47 patients with benign prostatic hyperplasia (BPH). The participants were randomly assigned to 3 study food trial groups: a placebo group (0 mg extract per day); a lower-dose group (160 mg PE per day); and a high-dose group (320 mg PE per day) (Groups P, L, and H, respectively). Outcome measures were the change during the 12-week intervention period in subjective symptom scores and 2 urodynamic parameters, maximum flow rate (Q max) and residual urine volume. Q (max) values were significantly increased in group H ($P < 0.05$) but not in groups L or P. While residual urine volume was significantly increased in groups L and P ($P < 0.05$ each), the level in group H decreased, although the difference between groups H and P did not reach statistical significance (P=0.052). No pollen-related health hazards or laboratory abnormalities of clinical significance were found. The results can be summarized that a higher dose of bee pollen extract intake significantly decrease the symptoms of BPH [104].

Dogs with BPH were successively treated with doses of 5-10 g/kg bee pollen for two months[93].

Biologically active substances

Besides the above mentioned hydoroxamic acitivity there are other substances. Quercetin is one of the main flavonoids in bee pollen [22]. This compound shows in vitro a permanent inhibition of androgen-independents cancer cells PC-3 at the dose of 100 µM. In prostate cancer cells this activity is due to the ability of quercetin to block the cell cycle in various phases through an inhibition of the expression of several specific genes. Quercetin also up-regulates expression of various tumour suppressor genes while down-regulating oncogene expression [110]. In a prospective, double blind, placebo-controlled trial, the patients who had been taking quercetin (500mg, 2 time/day for 4 weeks) showed a significant improvement in NIH chronic prostatitis symptoms, 67% of the patients taking quercetin having a significant decrease of symptoms [140].

Rutin, a principal pollen constituent has antitumor properties has similar antitumor activity as quercetin. These two substances have been recognised to act against apoptosis (programmed cell death) and thus delay cancer growth[77].

Kaempferol, another bee pollen flavonoid caused a reversible inhibition of PC-3 cancer cells growth [60]. It is known that other flavonoids present in pollen (e.g. apigenin) are able to depress the kinase activation in prostate cancer [91].

Another class of substances that might be involved in the antiprostatitis action of bee pollen are the **phytosterols**. Besides cholesterol other sterols in pollen are fucosterol, beta-sitosterol, stigmasterol and campesterol. Like other components the amounts and sterol types vary depending on the plant species [146]. Beta-sitosterol is known to be an active substance against BPH [80].

A third group involved in the antiprostatis activity is **beta- carotene**. The antiprostatitis and anti prostate cancer is evidenced for lycopene. A drop of PSA, an indicator of prostatitis and prostate cancer has been evidenced by Cistus and willow pollen, both pollen rich in carotenes, but not by chestnut pollen, having a relatively low beta-carotene content [118]. Beta carototene decreases the risk for some prostate carcinoma[33]

Hay fever and other allergies

Air born pollen is known to cause allergic reactions (see allergy section). However, there are promising results that pollen can also be used to prevent these allergies. Claims that a small consumption of bee pollen can desensitise against hay fever are known since a long time. However, only recently it was proven that bee pollen indeed exerts antiallergic and anti-hay fever effects.

The antiallergic activity of bee pollen phenolic extract (BPPE) and the flavonoid myricetin (MYR) was tested in a murine model of ovalbumin (OVA)-induced allergy in mice. BPPE (200 mg/kg) and MYR (5 mg/kg) treatments showed inhibition of different allergic reactions. The results support the hypothesis that MYR is one of the flavonoids of BPPE responsible for the anti-allergic effect and a potential tool to treat allergy [100].

Since mast cells play a central role in the pathogenesis of various allergic diseases, the effect of bee pollen ingestion by rats significantly reduced the cutaneous mast cell activation elicited specific antigens. It also reduced in vitro mast cell degranulation and tumour necrosis factor-X production. These results revealed that the antiallergic action of bee pollen was exerted by inhibiting the activation of mast cells, which plays important roles, not only in the early phase, but also in the late phase of the allergic reaction [66].

Grass pollen is promising agent for treatment of persons suffering from allergies towards grass pollen allergy [73, 159] but also following bee stings[51, 113]. In a clinical test with children allergic to grass pollen extracts of pollen were administered orally and subcutaneously, last treatment being the the most efficient [127]. Application of special grass pollen tablets was also successfully tested[86]

Recently pollen vaccines have been prepared from pollen, from which allergenic components were removed. In a recent publication a successful clinical trial in of the sublingually applied *Gramineae* pollen vaccine against hay fever of humans has been reported [101]. A successful therapy with a pollen based vaccine against birch delivered sublingually and subcutaneously has also been reported [78]. These results are very promising due to the fact of increased incidence of hay fever in the developed countries.

Aqueous pollen extract has been successfully used against house-dust asthma [167]. A preparation from different bee pollen, called Pollysat was also used for decreasing the symptoms of hay fever [128].

Homeopathic grass pollen preparations has been successfully tested against hay fever[79, 148]

Hepatitis

Bee pollen against hepatitis, after Asafova et al.[7] and Shkenkderov and Ivanov[139]

Author, clinical test,	Pollen intake, recommendation, results
Ialomicianu et al. 1976 110 deteriorating chronic hepatitis patients	Intake of 30 g bee bread or fresh pollen daily: 90 days pollen or 30 days bee bread. Normalisation of albumin/globulin blood ratio. In patients taking bee bread the ratio changed from 0.96 to 1.27 while in patients taking pollen from 0.85 to 1.26.
Belyaeva et al. 1990 Children virus hepatitis	Children from 3 to 5 years: 12 g , 6-12 years: 16 g, pollen as water suspension or with honey. In comparison with controls significant changes of white and red blood bodies, of plasma proteins and of the humoral immune response
Bashmakov and Chernov 1986 Chronic hepatitis and jaundice	Children: 3 times one tablespoon, grownups 3 times one soupspoon. 1 month after the operation, improvement of patients.
Uzbekova (2001), Hepatitis B	Successful use of bee pollen [157]

Antiaging

The health enhancing effects of pollen in cardiovascular health (see above) and also its anabolic, growth stimulating properties (page 6) make it a good candidate for treating age-connected conditions such as arteriosclerosis and chronic fatigue. Ludyanski has applied pollen successfully in geriatrics and against chronic fatigue (see below).

The effect of intake of a total of 40 g bee pollen was tested twice daily for 1 month on 28 patients with an average age of 72 years with cholesterosis and cholesteatosis of the gall bladder. In 86 % of the patients the cholesterol values decreased from 7.8 mm/l to 5.9 mm/l. In 62 % of the patients the gall bladder secretion improved, with an improved consistency, while in the rest of the patients there was no improvement[39].

In the monograph of Asofova et al. [7] successful treatments were reported for:

- Climacterium for men and women: 50 g pollen and 100 g of honey daily (Ohotsky, Kostish, 1978)
- Chronic weakness (asthenia): long-term intake of 1 g daily

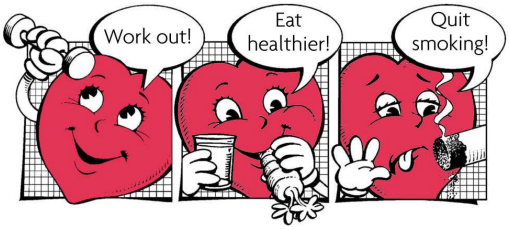
Better memory

In traditional Chinese medicine a mixture of bee pollen, radix polygoni multiflore, *Ziziphi spinosae* semen, *Radix salviae multiorhizae*, *Fructus schisandrae* and *Fructus ligustris lucidae*, known as “NaO Li Su”, has reputation as a medicine against declining memory functions. In the present study the effect of this mixture on failing memory was assessed in 100 elderly Danish volunteers by a double-blind placebo controlled cross-over trial. The effect was evaluated after treatment periods of 3 months duration by a battery of psychological and biochemical tests. No desirable effects on memory functions were achieved with this treatment. Increases in the number of red blood cells and in the serum creatinine levels were seen after treatment. In the subgroup initially showing a number of red blood cells below the median a significant positive correlation was found between changes in the number of red blood cells and changes in the Wechsler Memory Scale scores [67].

Menopause

An daily ingestion of table spoon of pollen (about 10 g) for a period of 14 days by breast cancer patients improved the menopausal symptoms of 70 % of the patients, while a placebo effect of 25 % was expected[103]

Heart and blood circulation diseases

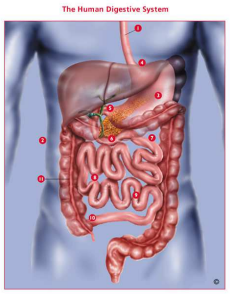


Different clinical studies with bee pollen

As reported in different monographs [7, 139, 171] or after original references

Author, clinical test, disease	Pollen intake, recommendation, results
Dudaev et al, 1988 Ischemic disease after myocardial infarct	2 teaspoons 3 times a day. Significant effects in blood values: fall of cholesterol, fibrinogen, soluble fibrin and of blood viscosity. (after[7])
Bashmakov and Chernov 1988 55 patients after heart surgery or with myocardial infarct, unknown number of patients with other heart diseases	Pollen in honey 1:1, dissolved in 100 ml of water 3 times a day before meals, for 3 months, in connection with standard medication. Treatments were successful. (after[7])
Golovkin et al. 1993 Ischemic disease after myocardial infarct	Suppositories with 1 g pollen, twice a day; after 12 days examination: positive effects on myocardial metabolism haemodynamics and resilence. (after[7])
Balshushkiavich et al, 1986 Ischemic disease after myocardial infarct	40 g pollen: twice a day two tablespoons: recommendation to include pollen in diet in connection with physio-and sport therapy. (after[7])
Koslic and Takac, 1979 5 Arteriosclerosis patients with increased triglyceride content	Intake 2 times 2.5 pollen, measurement in blood in two weeks triglyceride content fell to half the initial (2.44 mM/l) while Changes in the levels of lipoproteins and cholesterol were not significant (after [139])
Georgieva and Wassilev, 1976 60 elderly patients with arteriosclerosis and 40 with brain arteriosclerosis	1 tablespoon pollen before meals, twice a day for 1 month. A small fall of cholesterol and lipoproteins in arteriosclerosis patients and improvement of non dynamic neurasthenia disorders of brain arteriosclerosis patients (after [139])
Kassaynko, 2010, [74] Treatment of adult patients with dislipidia	Intake for 12 weeks of 40 g daily pollen or bee bread resulted in cholesterol decrease by 11.4, resp. 20.5 %; the same quantity of bee bread decreased triglicerides by 12.5 % and HDC by 14.3 %
Stasitite and Vassilauskas, 2006 Treatments of adult patients with dislipidemia	Intake for 30 days of 2x daily 4.5 g pollen for 30 days results in a decrease of cholesterol and β lipoproteins, biggest decrease in smoking women by 30.8, resp. 12.8 %. (after[171])
Liferov et al. 2009[92] Treatment of patients with arterial hypertension	Treatment of 57 patients (men and women) for 45 days by intake of 2 x 15 g intake of bee bread daily. Total cholesterol decreased by 24 %, LDL by 36 %, HDL increased by a factor of 2.1.

Gastroenterological disorders



Different clinical studies with bee pollen

reported in the monographs of Asafova et al.[7] and Shkenkderov and Ivanov[139] as

Author, clinical test,	Pollen intake, recommendation, results
Lenormand and Chauvin, 1957 diarrhoea, colitis, enteritis, and chronic constipation	good treatment results
Georgieva, Vassilev, 1971 40 patients with bleeding stomach ulcer, controls: only anti-bleeding drugs	Two soupspoons pollen per day for 10 days, bleeding stopped after 2-4 days while in the controls bleeding stopped after 10 days
Krikshtopaitis et al. 1986 stomach ulcer (n=7) duodenal ulcer (n=17) and 45 patients with different disorders	5 g pollen in honey 1:1, 3 times a day with 100-150 ml boiled water half an hour before meals for 2-4 weeks. Quick healing of all but one patients (this patient had nausea after pollen)
Krikshtopaitis and Yudovalkis 1988 Chronic duodenal and gastric ulcers	5 g pollen in honey 1:1, 3 times a day for 4-5 weeks. Stomach pH rose from 1.1 to 5.0; erosions healed and acidity was normalised
Prieditis et al. 1986 After chirurgy of duodenal and gastric ulcer	15 g pollen in half a glass of water twice a day after breakfast and lunch for 10 days. Dispepsia disappeared, positive effects on duodenal motor

patients	skills, serum and hepatic values normalised
Balshushkiavich et al, 1988 Duodenal ulcer, gastritis	2 times per day10 g pollen for 10 days, together with a diet and physical exercises
Bashmakov and Chernov, 1988 Duodenal and gastric ulcers, colitis	Pollen in honey 1:1, 3 times a day: initial 5 days tablespoon, then 5 days with dessertspoon and finally with soupspoon for 1-2 months; improvement, measured with gastric acidity decrease
Ivanova, Djarimov, 1993 Duodenal and gastric ulcer	One table spoon pollen in honey 1:2 for 3 times a day one hour before meals. Significantly better results than controls.

The experience of Ludyanski

Ludyansky, a chief doctor in a big Russian hospital, with life-long practice in apitherapy, has summarised the apitherapy knowledge in his monography “Apitherapia” (in Russian)[64]. He summarises the medical uses of pollen in his hospital in the following table:

Treated disease	Very good and good improvement	No improvement
Aneamia	26	5
Geriatry	23	-
Impotency	50	15
Gastritis	47	5
Posttraumatic asthenic syndrome	81	15

Ukranian pollen preparations against different diseases

The Ukranian pharmacist Tikhonov and his group from the National Pharmacy University of the Urkaine developed a number of bee pollen preparation (water and organic solvents)and tested them against a number of diseases[152]

Digestive diseases in mice and humans

The preparation **Pollenzym** is a preparation based on a water extraction from pollen and contains proteins, enzymes and amino acids. It was successfully tested with mice. It improves the microcirculation of the intestines and can heal following digestive diseases: chronic entercolitis, pancreatitis, hepatitis and gall bladder inflammation.

The same preparation was used in the following manner against a number of digestive diseases: 4 times daily one pill after the meals, for 15-20 days. A test with 30 humans with infestations of the small and the large intestines showed only improvement of the small intestine inflammation. In a test with 39 diseased humans with chronic pancreatitis were treated. After 5 to 7 days symptoms like burping and stomach inflation diminish, after 8-9 days also other symptoms were improved. The preparation was also successfully tested with 40 humans with chronic gastroduodenitis (gastric ulcer). After 10 days the majority of the patients had improved significantly. The preparation was also successfully tested with 60 patients having a gall bladder enlargement, the gall bladder decreased in size. The preparation was also successfully tested with patients having a chronic pancreatitis.

The lipophylic extract of pollen (**LEOP**) is an exctract prepared with non-polar solvents and plant oils. It contains beta-carotin, flavonoids, lipids, fatty acids and fat soluble vitamins. This preparation is non toxic according to different toxicity and allergenity tests if applied in animals until a dose of 40 g/kg. LEOP is applied as a suppositoria **Polenfen.** Tested in mice this preparation causes improvement of sexual disfuctions and an increase of sexual activity. According to the results the preparations can be used in the treatment of sexual disfunctions connected with androgenic insufficiency and inhibited ejaculation, hemarroids and proctitis. The suppositoria **Polenfen** are applied twice a day for 15-30 days.

Another preparation **Pollentar** is based on a pollen extract and succinic acid. This preparation was successfully tested in mice for use for the increase of performance under the conditions of physical strain. This is due to its anti-hypoxic activity, resulting in increased performance. It has also a brain blood circulation protecting activity as tested positively in mice with brain ischemia (blood insufficiency in the brain).

Other therapeutic effects

Bee pollen

Bee bread (as only medicine) was administered to 20 patients suffering from anaemia. For more than a month one teaspoon of pure bee bread (or a 1:1 mixture of bee bread and honey) was administered to adults (1/3 teaspoon to children up to a year; ½ teaspoon for children from one year onward) three times a day. The health condition of the inpatients improved during the therapy. The patients appetite increased, they were more lively, better humoured und gained weight. Furthermore, their headings reduced and their debility, vertigo and tiredness receded as well. Epidermis and mucous membranes were less pale and the haemoglobin and their number of erythrocytes increased. Referring to the results the paper states that bee bread is suitable for the treatment of anemia.[89] A Bulgarian report support these findings [53]

Bee pollen was ingested by 10 patients suffering from hypertriglyceridemia which were under permanent kidney dialysis. After 2 weeks the level of serum triglyceride dropped and after 2 months it reached normal values. The authors conclude that the positive pollen effect can be used for the treatment of hypertriglecyridia and possibly also of uricaemia [83].

Cancer, radiation

Bee pollen was effective in reducing adverse effects of radiation used for cancer treatment in a double blind study of 25 women with inoperable uterine cancer[105].

In Chinese medicine bee pollen is used for blood formation, reducing cravings for sweets and alcohol, as a radiation protectant and a cancer inhibitor[156].

In Russia it was shown that ingestion of whole bee pollen or pollen tablets or its extracts reduced of brain hypoxia, protecting against ionizing radiation, acting against stress and tumour of humans. The strong adaptogenic activity exhibits pollen load in natural or powdered form (tablets, capsules) while the aqueous and ethanol extracts had a lower adaptogenic activity. For the enhancing of physical and immunological resistance higher doses of pollen load (10-40 g daily) and for enhancing of mental condition the lower doses of this product (1-3 g) during 2-6 weeks should be used[75].

The introduction of a pollen diet as an adjuvant in the reduction of side effects during radiotherapy of patients with gynaecological cancer (15 women with carcinoma of the cervix) received a pollen diet during irradiation, whilst ten further patients receiving irradiation served as controls without pollen added to the diet. Serum enzymes, proteins, vitamins and blood count were analysed before and after irradiation. It appears, that pollen favourably influences the efficacy of irradiation and reduces the frequency of side effects, both subjectively and objectively[63].

Other effects

In the monograph of Asofova et al. [7] successful treatments were reported agaubst chronic bronchitis: 3 times a day a soup spoon of honey:pollen 5:1 mixture (Chuhrienko et al. 1993; Bashmakov and Chernov, 1988)

Flower pollen

Therapy-relevant research has been carried mainly with different flower pollen preparations: Cernitol, Cernitron and Cernitin. Pollen extracts are reported to produce good results in patients suffering from nutritional problems in the form of emaciation, loss of appetite and physical and mental asthenia. These effects have been noted both in children and elderly patients convalescing after various illnesses. In particular, protein synthesis increased as did secretion of 17-OH-steroids and 17-oxi-steroids. No side effects being attributed to the Cernitrin intake were shown as being attributed to the preparation, and significant results were achieved after as little as two months of treatment [38, 90].

Mixed pollen containing four sorts of pollens (Rape, Typhae, Corn, Sunflower) is capable of increasing body tolerance to acute hypoxia and promoting adaptation to highlands. The experimental study showed that pollen can significantly increase body tolerance to acute hypoxia pollen can also increase the high energy content and normalize the activity of several enzymes which are important to high energy metabolism; regulate the neurotransmitter in 4 parts of the brain and maintain normal activities in the nervous system; increase the secretion of adrenocortical hormone which may favour O2 absorption; increase SOD content in tissues (heart, liver) and hence may prevent super-oxygenation and guard against free radicals, increase PO2 in the brain and arterial blood; decrease oxygen consumption and blood lactic acid concentration; and increase the immunity of animals under

normal condition. In field study, carried out with humans in two different years it was shown that humans, taking pollen 3 to 5 days before moving to 5000 m showed no or less symptoms that individuals who had taken other or no drugs. The researchers concluded that pollen intake can also reduce and ameliorate symptoms of acute mountain sickness [117].

SPECIFIC THERAPEUTIC OF UNIFLORAL POLLEN

In almost all scientific studies mixed pollen was used. As pollen composition varies widely depending on the type of pollen, specific pollen should be used in medicine.

The effects presented in the data below are not based on scientific or clinic studies but are based on traditional folk medicine. These effects should be tested in clinical studies.

Therapeutic properties of different pollen types in folk medicine after[18, 29]

Therapeutic effect	Pollen type
Antibiotic	Eucalyptus, maize, chestnut, dandelion, clover
Improves blood circulation	Cherry, horse chestnut, sweet chestnut, willow
Calming, against sleeplessness	Acacia. citrus, hawthorn, linden, poppy,
Cough	Poppy
Diuretic	Dandelion, cherry, cornflower
Digestive	Acacia, lavender rosemary
Heart fortification	Hawthorn
Improvement of liver function	Horse chestnut, sweet chestnut, dandelion
General tonifier	Apple, eucalyptus, willow
Ulcer healing	Rape

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SIDE EFFECTS AND ALLERGIC REACTIONS

Allergy

Bee-pollen is normally well tolerated, but the presence of allergenic pollens and substances can not be excluded. Pollen allergy like hay-fever, concerns mainly allergy against air-born pollen, while allergies to ingested pollen are relatively rare, with a similar rate as other foods. A case of a 34-year-old Spanish woman with a lifelong history of seasonal rhinoconjunctivitis and honey intolerance which developed eosinophilic gastroenteritis after ingestion of bee pollen [123]. Non-life-threatening anaphylactic reaction has been recorded after bee pollen intake [54, 55].According to a 2008 Russian study the incidence to pollen ingestion, tested in 891 normal humans was 1.45 % [143].

About 10 to 25 % of the population has hay fever or other forms of airborne pollen allergy. The allergenic effects of bee pollen have been reviewed [42, 153]. The allergy towards ingested bee pollen has been reviewed in 2015 by Choi et al. Mostly the allergy reaction is due to wind pollinated pollen but there are bee pollen from the Compositae family which can also induce an allergy[31]

Allergy after ingestion of pollen of the composite family was reported [32]. A case of a 34-year-old Spanish woman with a lifelong history of seasonal rhinoconjunctivitis and honey intolerance which developed eosinophilic gastroenteritis after ingestion of bee pollen [123]. Non-life-threatening anaphylactic reaction [54, 55], and also one case of renal failure [2] and one case of anaphylactic shock[69] have been recorded after bee pollen intake.

For safety reasons it is recommended that people who are susceptible to allergies or asthma, or people with hay fever should avoid intake of bee pollen.

But: bee pollen has an anti-allergenic effect[66], there is a successful desensitisation therapy to hay fever by pollen, see section **Hay Fever.**

Toxic compounds and microbiological contaminants

Trace amounts of hepatotoxic pyrolizidine alkaloids (PA) were found in pollen of *Echium vulgare, E. plantagineum, Senecio jacobaea, S. ovatus, and Eupatorium cannabinum* [116]. In Middle and Northern Europe these pollens are not among the main pollen gathered by bees, however in Southern Europe the two *Echium* plants are more diffused and are gathered by bees in larger amounts [16, 93].

Recently Kempf et al. (2010) reviewed the importance of PA's for human nutrition. The quantities found in Echium, Senecio, Eupatrium and Phalaenopsis pollen varied between 0.8 and 14 mg/g [76].

Pollen should be tested to fulfil with standards for microbiological purity and to residues of contaminants. The allergy issue will be addressed later. The different contaminants of bee-pollen have been recently reviewed [8].

Pollen intake

Whole pollen

From biological point of view the most effective pollen forms are bee bread and fresh frozen pollen. As pollen is relatively an expensive food product, a regular uptake of 10 g (2 teaspoons) is realistic and can have a prophylactic effect. For prophylactics and health enhancing a dose of 10-20 g per day can be taken for a longer period of time, best twice for 3 months a year, e.g. during winter. For apitherapy the dose of pollen to be taken by adults is 20-50 g daily, taken 3 times per day, 1-2 hours before meals.

For improving pollen digestibility place pollen in water overnight. Good chewing or milling of pollen before administering improves the digestibility too. In order to counterbalance the bitter taste of pollen, 1 part of pollen can be mixed with 1 part of honey (by weight).

Approximate weight of pollen given as spoons: teaspoon 6 g; dessertspoon 9 g; soupspoon 12 g.

Cracked pollen and pollen extracts

Another intake forms are cracked pollen and bee pollen extracts. Cracking of pollen increases its digestibility. Bee pollen extraction improves the antioxidant activity, best extraction is achieved with ethanol[85]. Maceration with water increases the pollen digestibility, for several hours or overnight.

It was found out that ethanol extracts of pepsin digested pollen have a higher antioxidant effect than ethanol extracts of normal pollen, pepsin digested pollen had the lowest antioxidant effect[132]

CONCLUSION: BEE POLLEN AS A FUNCTIONAL FOOD

2. Health claims

According to the EU Regulation 1924/2006 [48] different health claims can be made for food:

1. **Physical performance and fitness**

Long term ingestion of pollen and special pollen preparations (cracked pollen, pollen extracts) can improve the physical performance and fitness of sportsmen and elderly people

2. **Gut, digestion and liver health**

P*ollen intake can improve gut, gastroenterological and liver health*

Fresh frozen pollen conserves best the biological properties of pollen

Bee bread for optimal digestibility and bioavailability of pollen ingredients

Pollen in honey combines the functional properties of the two products.

Pollen extracts or tablets are used for intake of easily digestible pollen component supplementation.

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