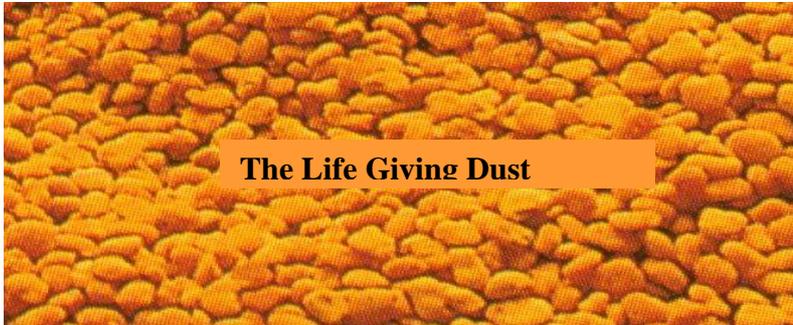


# Pollen: Production, Nutrition and Health: A Review

Stefan Bogdanov



tiger lilly pollen, courtesy [www.pbrc.hawaii.edu](http://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 physicians 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 aphrodisiac, also beneficial for the stomach, giving back the fervour of the blood and curing swellings produced by eating certain foods<sup>36</sup>.

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.

## OPTIMAL PRODUCTION



Fresh, bee collected pollen contains about 20-30 g water per 100 g. This high humidity is an ideal culture medium for micro-organisms like bacteria and yeast. For prevention of spoilage and for preservation of a maximum quality the pollen has to be harvested daily and immediately placed in a freezer. After two days of storage in the freezer, the pest insects will be killed<sup>14</sup> After thawing pollen can be kept only for a few hours and should be further processed as soon as possible.

## Drying

The pollen is best dried in an electric oven, where humidity can continuously escape. Then it is purified by a special machine, similar to a seed cleaning machine. The maximum temperature is 30°C and the drying time should be as short as possible in order to avoid vitamin losses.

Fresh, bee collected pollen contains about 20-30 g water per 100 g. This high humidity is an ideal culture medium for micro-organisms like bacteria and yeast. For prevention of spoilage and for preservation of a maximum quality the pollen has to be harvested daily and immediately placed in a freezer. After thawing pollen can be kept only for a few hours and should be further processed as soon as possible. After drying the water content should be 6 g water per 100 g pollen.

Today pollen is dried generally in electric ovens, where humidity can continuously escape. The prescribed maximum temperature was 40°C. However this temperature seems to be high. The effect of different methods of preservation (freezing, drying at about 40°C and lyophilisation) on selected parameters attributed to the biological quality of bee pollen were tested in Poland. Freezing caused no substantial changes in the chemical composition of the pollen loads, so this technique should be recommended when the preservation of the pollen load for nutrition or therapeutic purposes is important. Lyophilisation markedly decreased vitamin C and provitamin A content, but drying at 40°C revealed the most disadvantageous effect<sup>171</sup>.

A Brazilian study found that pollen drying for 6 hours at 45 °C led to significant losses of vitamin E and β-carotene, as well as pro-vitamin A by 15 to 25 %<sup>38</sup>

A Spanish study showed that freeze drying is better for the preservation of the chemical and the biological properties of pollen than oven-dried one<sup>41</sup>

A Portuguese study revealed that quick drying of bee pollen (3 times for 45 seconds) at 50° C in an infra-red oven did not lead to losses of anti-oxidant activity

Concluding the above results, pollen should be dried at possible low temperatures, a maximum of 30 °C. The better alternative is to use freeze drying. A pollen freeze drying machine is described in the literature<sup>55</sup>, but its effect on pollen quality has not been tested.

## Storage

Experience in Switzerland showed that from a microbiological and sensory point of view pollen remains stable until 1.5 years of storage at room temperature. Under these conditions pollen keeps its sensory and microbiological quality for a storage period of 2 years, if stored in a cool, dry and dark place<sup>15</sup>.

As a functional food one of the main health enhancing properties is the strong antioxidant activity of pollen.

Pollen loses a considerable amount of its antioxidant activity (about 59%) after one year<sup>26</sup>. This loss might be due to the decrease of phenolic compounds, observed in another study<sup>150</sup>

The amounts of four out of nine constituents examined (reducing sugars, total proteins, vitamin C, and provitamin A) markedly decreased upon storage. Taking into account the methods of production practical recommendations for the means of preservation and optimum conditions for the storage of pollen loads are suggested. Freezing followed by storage at -20°C in pure nitrogen guarantees high biological qualities of bee pollen kept for up to 6 months. Pollen stored for a longer periods should, however, be dried by lyophilisation and stored at -20°C in pure nitrogen to preserve its highest biological activities. Storage of pollen at 0 to 10 degrees in vacuum has been proposed in order to prevent antioxidant spoilage<sup>166</sup>.

A Brazilian study found no loss of vitamin C and losses of vitamin E and beta-carotenes by 15 to 20 % upon storage of dry pollen for one year at room temperature<sup>39</sup>

Fresh, frozen purified pollen should be stored under nitrogen until consumption for preservation of optimal biological and nutritive properties<sup>132</sup>.

## Harvesting of unifloral pollen

Normally beekeepers collect mixed pollen. Harvesting of unifloral pollen is important because only this type of pollen has constant composition and thus can be successfully used in nutrition and medicine. A machine was constructed in Austria, by the help of which bee pollen can be sorted into different types, the purity of the sorted pollen being about 90 %<sup>144</sup>.

## Fresh freeze-dried pollen



Patrice Percie du Sert from France invented and patented a technique in 1994 that allows all the nutrients in fresh bee pollen to be preserved. The pollen is frozen at collection and packed in a nitrogen filled package; oxygen is excluded, eliminating decay. This process allows the pollen to be presented as close to its pure state as possible. Fresh, purified pollen can be frozen and stored under nitrogen until consumption for preservation of optimal biological and nutritive properties<sup>132</sup>

## Bee bread



Bees store pollen in the hive as bee bread. Pollen is mixed with honey and bee secretions and stored in the combs. Bee bread undergoes a lactic acid fermentation and can be thus preserved. Bee bread combs will often be sold as a whole. For that purpose a bee queen separator is placed between brood and honey combs during a period of a maximum pollen gathering activity. When the combs are full, the pollen is harvested by means of a scraper and filled into a jar.

### Production of “home bee bread” after Dany 1988, as described by [Krell<sup>95</sup>](#)

*The term “bee bread” is reserved for the original bee pollen stored in the combs. Thus, the product described below cannot be called “home bee bread” or fermented pollen.*

*Normally, the term bee bread refers to the pollen stored by the bees in their combs. The bee bread has already been processed by the bees for storage with the addition of various enzymes and honey, which subsequently ferments. This type of lactic acid fermentation is similar to that in yoghurts (and other fermented milk products) and renders the end product more digestible and enriched with new nutrients. One advantage is almost unlimited storability of bee bread in comparison with dried or frozen pollen in which nutritional values are rapidly lost. The natural process carried out by the bees can more or less be repeated artificially with dry or fresh bee-collected pollen. It is important however, to provide the correct conditions during the fermentation process.*

#### The container

*Wide-mouthed bottles or jars with airtight lids are absolutely essential. Airtight stainless steel or glazed clay pots can also be used. Containers should always be large enough to leave enough airspace (20 to 25 % of the total volume) above the culture.*

#### The temperature

*The temperature for the first two to three days should be between 28 and 32<sup>0</sup>C; the bees maintain a temperature of approximately 34<sup>0</sup>C. After the first two or three days the temperature should be lowered to 20<sup>0</sup>C.*

*The high initial temperature is important to stop the growth of undesirable bacteria as quickly as possible. At this ideal temperature all bacteria grow fast so that an excess of gas and acid accumulates. Only lactic acid producing bacteria (lactobacilli) and some yeasts continue to grow. The former soon dominate the whole culture. This final growth of lactobacilli should proceed slowly, hence the reduction in temperature after 2-3 days.*

#### The starter culture

*It is best to start the culture with an inoculation of the right bacteria such as Lactobacillus xylosus or lactobacilli contained in whey. Freeze-dried bacteria are best if they can be purchased, but otherwise, the best cultures are those that can be obtained from dairies. Whey itself can be used. If the whey is derived from unprocessed fresh milk it should be boiled before use. A culture can also be started with natural bee bread.*

#### Preservation

*Fermentation produces a pleasant degree of acidity (ideally pH 3.6-3.8). Some pollen species may promote excessive yeast growth but this does not spoil the bee bread. If the flavour is strange or some other mildew-like or unpleasant odours arise from the bee bread, discard it and try again. The final product, can be stored for years, once unsealed, it can be dried and thus is storable for many more months.*

#### General conditions

*For successful fermentation, exact quantities are less important than the correct conditions:*

- the pollen to be fermented needs to be maintained under pressure
- the air space above the food needs to be sufficient (20-25 % of total volume)
- the container needs to be airtight
- the temperature should not drop below 18<sup>0</sup>C

#### **Ingredients (in parts by weight):**

*10 Pollen; 1.5 Honey; 2.5 Clean water 0.02 Whey or very small quantity of dried lactic acid bacteria  
Clean and slightly dry the fresh pollen. If dried pollen is used, an extra 0.5 parts of water is added and the final mix soaked for a couple of hours before placing it in the fermentation vessels. If the mixture is too dry, a little more honey-water solution can be added.*

Heat the water, stir in the honey and boil for at least 5 minutes. Do not allow the mix to boil over. Let the mix cool. When the temperature is approximately 30-32 °C, stir in the whey or starter culture and add the pollen. Press into the fermentation container.

When preparing large quantities in large containers, the pollen mass should be weighted down with a couple of weights (clean stones) on a very clean board.

Close the container well and place in a warm place (30-32 °C).

After 2-3 days, remove to a cool area (preferably at 20°C). 8 to 12 days later the fermentation will have passed its peak and the beebread should be ready. The lower the temperature, the slower is the progress of fermentation.

Leave the jars sealed for storage.

## STANDARD AND QUALITY

From hygienic point of view the microbiological safety is the main quality criterion. It is important to control the microbiological quality of pollen, especially the absence of pathogenic germs and fungi. Destruction of bacteria by irradiation, ozone treatments<sup>203</sup> or chemical fumigants<sup>156</sup> is not necessary and leads to toxic residues..

For specific use the composition of biological active components e.g. flavonoids (Campos et al. 1997, Serra-Bonvehi et al., 2001) or vitamin content should be evaluated.

Pollen is the bee product, least influenced by contaminants from beekeeping<sup>14</sup>. However, it can be polluted by air contaminants, e.g. by heavy metals and pesticides. Thus, for optimum quality pollen should be gathered in areas which are at least 3 km distant from contamination sources such as heavy traffic and pesticide-treated agricultural areas.

In the last few years there are genetically manipulated plants and also pollen. No studies on the negative effect of such pollen on human nutrition have been published. The consumer should be aware of that. In the EU there is a compulsory indication of the content of genetically manipulated organisms (GMO) in food ( and also of pollen, if there the GMO content exceeds 1 %.

Analysis	Quality criteria
Sensory examination	Typical odour and taste, no visible contaminants
Microscopic examination	Origin test (botanical, geographical)
Microbiological testing	Bacterial load should be within legal hygienic limits
Chemical Examination	Water content: maximum 6 g/100 g pollen Content of main ingredients, carbohydrates, fat and protein, if labelled accordingly:
Contamination	Pesticides, heavy metals

### Sensory Analysis

Colour, appearance, odour and taste vary according to the botanical origin.

*Colour:* mostly yellow or yellow-brown, but many different colours are possible<sup>73, 89</sup>

*Appearance:* as so called „pollen loads“

*Odour:* hay-like

*Taste:* sweet, sour, bitter, spicy,

*Defects:* off-odour and taste, “molds”, fermented, rancid, visual impurities

### Microscopical examination

The pollen should not contain impurities like bee parts, wax, plant particles or other extraneous matter.

Pollen analysis can be used for the determination of the botanical origin. The same methodology, as used for pollen analysis of honey can be used<sup>107</sup>

There is no international standard. Some countries as Brazil, Bulgaria, Poland and Switzerland have national standards<sup>27</sup>. A proposal has been recently made<sup>27</sup>:

## Proposal for a chemical standard <sup>27</sup>

Component	Requirement	Content
Water content	not more than	8 g/100 g
Total protein content (N x 6.25)	not less than	15 g/100 g
Sugar content (total)	not less than	40 g/100 g
Fat	not less than	1,5 g/100 g

### Water content

The maximum allowed humidity varies from country to country: Brazil, 4 %, Switzerland, 6 %, in Russia: 8-10 %, Bulgaria: 10 %. More than 10 % makes the pollen susceptible to fermentation. The examination of the sensory quality in Switzerland concluded that humidity of less than 6 % makes the pollen too dry and less acceptable from sensory point of view.

The determination of pollen water content is carried out after drying to a constant weight in a cabinet dryer or infra-red oven drier <sup>61, 127</sup> or by Karl-Fischer method <sup>60, 158</sup>.

### Carbohydrates

Generally the carbohydrate content in g/ per 100 g will be determined by calculation, as the total carbohydrate content cannot be determined easily: 100 less the sum of water, fat, protein and ash content.

### Proteins and amino acids

Protein content is a standard determination after Kjeldahl, using a factor of 6.25 or 5.6 <sup>142</sup> (Rabie *et al.*, 1983). According methods for protein content in pollen loads we recommend to use for calculation (Kjeldahl method) N x 5.6 rather than N x 6.25 This factor is used by other authors too.

### Lipids

Lipids are determined by extraction with petrol ether <sup>170</sup>

### Contaminants

Pollen is the bee product that is most susceptible to pesticide contamination <sup>14</sup>. Pesticides should be tested whether they conform to the requirements. Also pollen should be tested for microbial purity.

## LABELLING

### Composition

The composition of pollen varies greatly depending on the botanical composition of the pollen. There are two possibilities.

1. Determine the composition of each lot and state the composition:
2. Indicate an average composition, example for Swiss pollen:  
100 g pollen contain on the average 20 g protein, 60 g carbohydrates 8 g fat and approx. 300 calories.  
Also the fiber content could be indicated,

**Serving:** 2 tea spoons daily (approx. 10 g); children: half dose.

**Warning:** It is recommended that people who are susceptible to allergies or asthma should avoid intake of bee pollen.

**Storage:** store in the dark in a cool dry place

**Best before** (valid after packaging of product)

Dried pollen stored at room temperature:

12 months

Dried pollen packed in vacuum:

24 months

Frozen fresh pollen stored in the freezer:

12 months



Storage in glass for one or more years results in decrease of antioxidant activity. Packing in vacuum or under N<sub>2</sub> is better.



Pollen packed in vacuum packed air-tight plastic bags prevents oxidation and decrease of antioxidant activity due to contact with oxygen.



Harvesting of unifloral pollen ensures constant and reproducible concentration of biologically active ingredients.

## COMPOSITION AND NUTRITION

**Pollen Composition and nutritional requirements: main components,** after <sup>23, 27</sup>

Main Components	g in 100 g	RDI* (g/day)
<b>Carbohydrates</b> (fructose, glucose, sucrose, fibers)	13 - 55	320
<b>Crude fibers</b>	0.3 – 20	30
<b>Protein</b>	10 – 40	50
<b>Fat</b>	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<sup>168</sup>. The sugars fructose, glucose and sucrose comprise about 90 % of all low molecular sugars<sup>157</sup>

### 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<sup>16</sup> while in pollen from France values between 9.2 and 14.4 g/100 g are reported<sup>133</sup>.

### 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<sup>146</sup>

### 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)<sup>168</sup>.

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.<sup>108</sup>

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) <sup>169</sup>

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 <sup>108</sup>. 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 <sup>169</sup>. The alpha-linoleic acid is a so called omega-3 acid, has many beneficial effects in nutrition <sup>162</sup>. 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

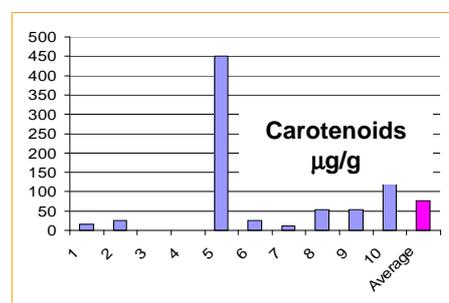
**Minerals and Nutritional Requirements**, after <sup>23, 27, 115</sup>

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 <sup>168</sup>. 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 <sup>70</sup>.

The sodium content of pollen is relatively low, values were found varying between 28 and 93 mg / 100 g <sup>12, 133, 160, 167</sup>.

### Vitamins and carotenoids



There is a significant nutritional contribution from most of the vitamins 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  $\beta$ -carotene, are related to vitamin. But these, too depend on the botanical source of the pollen, graph for pollen collected in Brazil after <sup>5</sup>. (graph left)

$\beta$ -carotene represents about 17 % of the totals carotenoids. French Cistus pollen contains 20 times more carotenoids than chestnut one <sup>133</sup>.

## Vitamins and Nutritional Requirements, after <sup>23, 27, 165</sup>

	mg in 100g	RDI (mg/day)
<b>Vitamines</b>		
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 vitamin A and significantly more pantothenic 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<sup>151</sup>.

Coenzyme Q was detected in pollen from China in quantities from 0 to 193 mg/kg<sup>196</sup>. The recommended daily intake of food supplements with Coenzyme Q is about 50 to 100 mg daily.

## 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<sup>168</sup>. 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<sup>26, 99</sup> the variation been due to variation of the flavonoid content of the different pollen types. Rutin seems to be the main flavonoid<sup>159</sup>. 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-sitosterol, stigmasterol and fucosterol, as well as 0.1 to 0.2 % mono-terpenes<sup>168</sup>.

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)<sup>134</sup>.

## Variation of pollen nutritional composition of several pollen gather in France after<sup>133</sup> 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

### Pollen digestion and pharmacodynamics



bioavailability<sup>145</sup>.

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<sup>146, 155</sup>. 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<sup>79</sup>. In in-vitro simulation of human digestion pollen was partly digested<sup>56</sup>, 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

Combination of protamex hydrolysis and ultrasonication can degrade the pollen coat and entirely disrupt both the exine and the intine of the pollen<sup>42</sup>

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<sup>96</sup>. 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 Ukrainian 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 **Ukrainian pollen preparations against different diseases**). Thus it seems 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<sup>105</sup>

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<sup>105</sup>

## 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<sup>31</sup>:

### Effects of pollen feeding on the weight increase of mice, after<sup>31</sup>

	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<sup>30</sup>:

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<sup>195</sup>

Mice feed with bee pollen from different plants for 6 months show an increase of the reproduction rates<sup>163</sup>.

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<sup>8</sup>.

Feeding of casein containing 5 % of pollen led 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<sup>175</sup>

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<sup>186</sup>.

### **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<sup>179</sup>.

### **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<sup>111</sup>. 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)<sup>192</sup>.

Experiments with sportsmen in Russia, reviewed by Asavova et al.<sup>7</sup> 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<sup>125</sup>.

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<sup>1</sup>. In another Russian study it was found that pollen intake by sportsmen in swimming and cross-country skiing leads to increased values of the haemoglobin and protein values<sup>139</sup>.

## FUNCTIONAL PROPERTIES



Parts of this section have appeared in<sup>23</sup>

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<sup>67</sup>.

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<sup>178</sup>.

**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-osteoporosis	Bee pollen
Anti-diarrhoe	Bee pollen
immunomodulating	Bee pollen
Probiotic and prebiotic	Bee pollen
Antiaging	Bee pollen,
Anti-anaemia	Bee pollen,
Antiatherogenic	Bee pollen, flower pollen
Positive influence on the urinary bladder of mice	flower pollen
Anti-depressant (inhibits MAO)	Bee pollen
Increases the immunity of broilers	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<sup>22</sup>.

In other study it was found that bee pollen hydrophobic compounds with unknown nature had antibacterial activity against *Viridans streptococci*<sup>174</sup>.

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 become a seed protectant because some of the bacterial pathogens are transmitted through the seeds<sup>11</sup>.

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<sup>52</sup>.

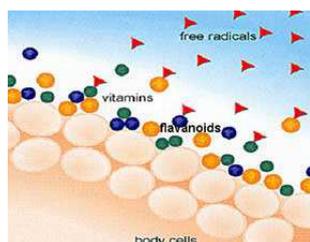
Pollen bread was found to possess an antibacterial activity against *Staph. aureus* and *S. epidermidis*<sup>9</sup>.

In a recent study with 80 % ethanol extracts of Brazilian pollen antibacterial activity was exhibited against *Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa* and *Klebsiella sp*<sup>28</sup>.

The antibacterial substances of pollen, active against *Streptococcus viridans* are similar to the ones found in propolis and honey combs<sup>174</sup>.

Pollen has also significant **antifungal** activity against different pathogens<sup>91, 128, 129</sup>

## 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<sup>135</sup>. 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<sup>25, 26, 98, 99</sup>. However the correlation between these two parameters is not that clear<sup>109</sup>. It was also found that the bee pollen antioxidant activity is pollen species-specific<sup>4, 54, 98, 99, 109</sup> and independent of its geographical origin<sup>4</sup>.

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<sup>109</sup>.

The values vary from: FRAP values, mM Fe<sup>2+</sup>/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<sup>130</sup>.

Bee bread was also found to have a high antioxidant activity<sup>10, 121</sup>.

The antioxidant abilities of *Cistus ladaniferus* 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  $\alpha$ -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)<sup>119</sup>.

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<sup>153</sup>

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<sup>26</sup>.

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<sup>46</sup>.

## 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<sup>135</sup>. 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<sup>13</sup>.

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<sup>6</sup>.

### **Hepatoprotection**

The effect of bee pollen on liver functions in old rats was studied. After one month they had a diminution of malondialdehyde levels and the sulphhydryl groups (SH-G) content was normalized. Also serum urea and protein levels were significantly improved at the end of the experiments<sup>182</sup>.

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<sup>50</sup>.

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<sup>51</sup>.

Paracetamol intoxicated rats fed 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<sup>80</sup>.

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*<sup>120</sup>.

Bee pollen of *Eucalyptus glob.* and *Salix. atr.* Showed antidiarrhetic activity in rats<sup>21</sup>

*Cardus*<sup>37</sup> and *castanea*<sup>201</sup> 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<sup>74</sup>. These effects could be explained by the pollen induced activation of the antioxidant system liver enzymes and the decrease of lipid peroxidation<sup>13</sup>.

### **Chemopreventive and anticancer activity**

The pollen flavonoids quercetin, rutin and chrysin have been shown to have a chemopreventive activity by increasing apoptosis (programmed cell death), thus acting in cancer prevention<sup>86, 136</sup>.

#### **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<sup>104</sup>.

A chloroform extract of Brassica bee pollen showed anticancer activity by increasing apoptosis of human prostate cancer PC-3 cells<sup>194</sup>.

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<sup>137</sup>.

Extracts of Turkish bee pollen inhibited respiratory burst of K-562 cancer cells<sup>3</sup>.

Bee pollen extracts inhibited the proliferation of human umbilical vein endothelial cells, but to a slighter extent than Chinese red propolis<sup>77</sup>

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<sup>185</sup>

### **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<sup>64</sup>. Another experiments with Cernithin extract showed that it had an anti-tumour activity of mice with lung cancer<sup>58</sup>

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<sup>205</sup>.

### **Anti-inflammatory 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 antiinflammatory 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 antiinflammatory, 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 cyclooxygenase and lipoxygenase activities<sup>32</sup>.

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<sup>110</sup>

## **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*<sup>66</sup>. The active factor of this effect, a bee pollen protein, has been characterised<sup>65</sup>.

It was shown by the same research group that water-solubilized extract from *Cistus ladaniferus* bee 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*<sup>198</sup>.

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<sup>199</sup>.

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 hypersensitivity<sup>45</sup>.

## 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<sup>188</sup>. Intake of bee pollen by rats induce a significant increase of the red blood cells<sup>30</sup>.

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<sup>69</sup>.

## Other effects

### Bee Pollen

#### *Antidiarrhoe activity*

Pollen extracts from bee collected *Eucalyptus 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, *Eucalyptus 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<sup>21</sup>.

#### *Immunomodulator*

Bee pollen is an immunomodulator.

It stimulates humoral immune response and changed the reaction of delayed-type hypersensitivity in rabbits<sup>45</sup>. 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<sup>140, 141</sup>.

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<sup>40</sup>

#### *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<sup>133, 134</sup>. Probiotic bacteria are found in bee bread<sup>183</sup>

#### *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<sup>81</sup>

#### *Antiaging and anti-neurodegeneration*

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<sup>106</sup>.

Polyphenols have anti Alzheimers and anti-Parkinson effects<sup>154, 187</sup> Chrysin a major pollen polyphenol is a potent anti-neurodegeneration agent<sup>118</sup>

#### *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<sup>204</sup>

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<sup>148</sup>

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<sup>148</sup>

#### *Anti-depressant*

Bee pollen inhibits the MAO enzyme, MAO inhibitors are generally used as anti-depressants<sup>202</sup>

#### *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<sup>92</sup>

### **Flower pollen**

Cernitin (a grass pollen preparation) has different beneficial properties: lowering serum lipid levels<sup>152, 190</sup> reducing atherosclerosis plaque intensity<sup>191</sup> and decreasing platelet aggregation both *in vitro*<sup>94</sup> and *in vivo*<sup>190</sup>. These assays have been confirmed in humans<sup>189</sup>.

Cernitin intake influenced positively the activity of urinary bladder of rats and mice<sup>122, 124</sup>.

## **POLLEN IN MEDICINE**

Some parts of the following section have appeared in<sup>23</sup>

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<sup>17</sup>.

A hydroxamic acid with anti-cancer *in-vitro* activity<sup>205</sup>, 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<sup>200</sup>.

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<sup>49</sup>.

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)<sup>173</sup>.

Cernitron was also tested in a study with 15 patients with chronic prostatitis and prostatic dysuria. In 13 of the patients there was either complete or lasting relief, 2 patients failed to respond<sup>19</sup>. Another double blind study showed a significant improvement of the Cernitron treated patients in comparison to the controls<sup>18</sup>. 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<sup>147</sup>.

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<sup>48</sup>.

The effect of the flower pollen on BPH 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<sup>29</sup>. This study is published in [www.graminex.com](http://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<sup>116</sup>.

Dogs with BPH were successively treated with doses of 5-10 g/kg bee pollen for two months<sup>104</sup>.

## Biologically active substances

Besides the above mentioned hydroxamic activity there are other substances. **Quercetin** is one of the main flavonoids in bee pollen<sup>24</sup>. This compound shows in vitro a permanent inhibition of androgen-independent cancer cells PC-3 at the dose of 100  $\mu$ M. 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<sup>123</sup>. 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<sup>161</sup>.

**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<sup>86</sup>.

**Kaempferol**, another bee pollen flavonoid caused a reversible inhibition of PC-3 cancer cells growth<sup>68</sup>. It is known that other flavonoids present in pollen (e.g. apigenin) are able to depress the kinase activation in prostate cancer<sup>102</sup>.

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<sup>168</sup>. Beta-sitosterol is known to be an active substance against BPH<sup>90</sup>.

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<sup>133</sup>. Beta carotene decreases the risk for some prostate carcinoma<sup>35</sup>

## 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<sup>112</sup>.

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<sup>75</sup>.

Grass pollen is promising agent for treatment of persons suffering from allergies towards grass pollen allergy<sup>82, 184</sup> but also following bee stings<sup>57, 126</sup>. 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<sup>143</sup>. Application of special grass pollen tablets was also successfully tested<sup>97</sup>

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<sup>113</sup>. A successful therapy with a pollen based vaccine against birch delivered sublingually and subcutaneously has also been reported<sup>87</sup>. 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<sup>193</sup>. A preparation from different bee pollen, called Pollysat was also used for decreasing the symptoms of hay fever<sup>145</sup>.

Homeopathic grass pollen preparations has been successfully tested against hay fever<sup>88, 172</sup>

## Hepatitis

**Bee pollen against hepatitis**, after Asafova et al.<sup>7</sup> and Shkenkderov and Ivanov<sup>160</sup>

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 soup spoon. 1 month after the operation, improvement of patients.
Uzbekova (2001), Hepatitis B	Successful use of bee pollen <sup>181</sup>

## 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<sup>44</sup>.

In the monograph of Asofova et al.<sup>7</sup> 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<sup>76</sup>.

## 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)<sup>72</sup>. 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

## Heart and blood circulation diseases

**Different clinical studies with bee pollen,** After monographs<sup>7, 160, 197</sup> or original references

Author, clinical test, disease	Pollen intake, recommendation, results
Dudaev et al, 1988 Ischemic disease after myocardial infarct Bashmakov and Chernov 1988 55 patients after heart surgery or with myocardial infarct, unknown number of patients with other heart diseases	2 teaspoons 3 times a day. Significant effects in blood values: fall of cholesterol, fibrinogen, soluble fibrin and of blood viscosity. (after <sup>7</sup> ) 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 <sup>7</sup> )
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 resilience. (after <sup>7</sup> )
Balshushkiavich et al, 1986 Ischemic disease after myocardial infarct Koslic and Takac, 1979 5 Arteriosclerosis patients with increased triglyceride content	40 g pollen: twice a day two tablespoons: recommendation to include pollen in diet in connection with physio-and sport therapy. (after <sup>7</sup> ) 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 <sup>160</sup> )
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 <sup>160</sup> )
Kassaynko, 2010, <sup>83</sup> 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 triglycerides by 12.5 % and HDC by 14.3 %
Stasite 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 $\beta$ lipoproteins, biggest decrease in smoking women by 30.8, resp. 12.8 %. (after <sup>197</sup> )
Liferov et al. 2009 <sup>103</sup> 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,** after.<sup>7</sup> and <sup>160</sup>

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 patients	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 skills, serum and hepatic values normalised
Balshushkiavich et al, 1988 Duodenal ulcer, gastritis	2 times per day 10 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 soup spoon 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.

## Ukrainian pollen preparations against different diseases

The Ukrainian pharmacist Tikhonov and his group from the National Pharmacy University of the Ukraine developed a number of bee pollen preparation (water and organic solvents) and tested them against a number of diseases<sup>176</sup>

### 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 enterocolitis, 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 extract 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 disfunctions 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

#### Anaemia

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; 1/2 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 and 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.<sup>100</sup> A Bulgarian report support these findings<sup>59</sup>

#### 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<sup>76</sup>.

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 hypertriglyceridemia and possibly also of uricaemia<sup>93</sup>.

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<sup>117</sup>.

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

In Chinese medicine bee pollen is used for blood formation, reducing cravings for sweets and alcohol, as a radiation protectant and a cancer inhibitor<sup>180</sup>.

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<sup>84</sup>.

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<sup>71</sup>.

## 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 Cernitron intake were shown as being attributed to the preparation, and significant results were achieved after as little as two months of treatment<sup>43, 101</sup>.

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 O<sub>2</sub> absorption; increase SOD content in tissues (heart, liver) and hence may prevent super-oxygenation and guard against free radicals, increase PO<sub>2</sub> 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<sup>131</sup>.



## SPECIFIC THERAPEUTIC OF UNIFLORAL POLLEN

Therapeutic properties of different pollen types in folk medicine after<sup>20, 31</sup>

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

The above effects are not based on scientific or clinic studies and no connection to specific constituents has been established until now.

## 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<sup>138</sup>. Non-life-threatening anaphylactic reaction has been recorded after bee pollen intake<sup>62, 63</sup>. According to a 2008 Russian study the incidence to pollen ingestion, tested in 891 normal humans was 1.45 %<sup>164</sup>.

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<sup>47, 177</sup>.

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<sup>33</sup>

Allergy after ingestion of pollen of the composite family was reported<sup>34</sup>. 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<sup>138</sup>. Non-life-threatening anaphylactic reaction<sup>62, 63</sup>, and also one case of renal failure<sup>2</sup> and one case of anaphylactic shock<sup>78</sup> 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<sup>75</sup>, there is a successful desensitisation therapy to hay fever by pollen, see section **Hay Fever**.

### Toxic compounds and microbiological contaminants

Trace amounts of hepatotoxic pyrrolizidine alkaloids (PA) were found in pollen of *Echium vulgare*, *E. plantagineum*, *Senecio jacobaea*, *S. ovatus*, and *Eupatorium cannabinum*<sup>116</sup>. 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<sup>16, 93</sup>.

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<sup>85</sup>.

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<sup>8</sup>.

## 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; soup spoon 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<sup>96</sup>. 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<sup>149</sup>

## CONCLUSION: BEE POLLEN AS A FUNCTIONAL FOOD

### 2. Health claims

According to the EU Regulation 1924/2006<sup>53</sup> 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

*Pollen 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.

## References

1. ABRAMOV, V V; BULAHOVA, E; CHERKASOVA, A; KULIKOVA, N (1993) Influence of natural products of beekeeping on the immune reactivity of sportsmen (in Russian) *Apitherapy and Beekeeping*, Vilnius; pp 167-173.
2. AKIYASU, T; PAUDYAL, B; PAUDYAL, P; KUMIKO, M; KAZUE, U; TAKUJI, N; TAKASHI, K; YOSHIHISA, N; MINORU, K (2010) A Case Report of Acute Renal Failure Associated With Bee Pollen Contained in Nutritional Supplements. *Therapeutic Apheresis and Dialysis* 14 (1): 93-97.
3. ALIYAZICIOGLU, Y; DEGER, O; OVALI, E; BARLAK, Y; HOSVER, I; TEKELIOGLU, Y; KARAHAN, S C (2005) Effects of Turkish pollen and propolis extracts on respiratory burst for K-562 cell lines. *International immunopharmacology* 5 (11): 1652-1657.
4. ALMARAZ-ABARCA, N; CAMPOS, M D; AVILA-REYES, J A; NARANJO-JIMENEZ, N; HERRERA-CORRAL, J; GONZALEZ-VALDEZ, L S (2004) Variability of antioxidant activity among honeybee-collected pollen of different botanical origin. *Interciencia* 29 (10): 574-578.
5. ALMEIDA-MURADIAN, L B; PAMPLONA, L C; COIMBRA, S; BARTH, O M (2005) Chemical composition and botanical evaluation of dried bee pollen pellets. *Journal of Food Composition and Analysis* 18: 105-111.
6. ANANEVA, T V; DVORETSKII, A I (1999) Effect of beta-carotene oil and bee pollen on ion transport in rat brain slices following radiation-chemical exposure. *Radiatsionnaia Biologiia, Radioecologiia* 39 (2-3): 341-344.
7. ASAFOVA, N; ORLOV, B; KOZIN, R (2001) *Physiologically active bee products (in Russian)*. Y.A.Nikolaev Nijnij Novgorod; 360 pp
8. ATTIA, Y A; AL HANOUN, A; EL DIN, A E T; BOVERA, F; SHEWIKI, Y E (2011) Effect of bee pollen levels on productive, reproductive and blood traits of NZW rabbits. *Journal of Animal Physiology and Animal Nutrition* 95 (3): 294-303.
9. BALTRUSAITYTE, V; VENSKUTONIS, P R; CEKSTERYTE, V (2007) Antibacterial activity of honey and beebread of different origin against S-aureus and S-epidermidis. *Food Technology and Biotechnology* 45 (2): 201-208.
10. BALTRUSAITYTE, V; VENSKUTONIS, P R; CEKSTERYTE, V (2007) Radical scavenging activity of different floral origin honey and beebread phenolic extracts. *Food Chemistry* 101 (2): 502-514.
11. BASIM, E; BASIM, H; OZCAN, M (2006) Antibacterial activities of Turkish pollen and propolis extracts against plant bacterial pathogens. *Journal of Food Engineering* 77 (4): 992-996.
12. BELL, R R; THORNBER, E J; SEET, J L L; GROVES, M T; HO, N P; BELL, D T (1983) Composition and protein quality of honey-bee-collected pollen of Eucalyptus marginata and Eucalyptus calophylla. *JOURNAL OF NUTRITION* 113 (12): 2479-2484.
13. BEVZO, V V; GRYGOR'EVA, N P (1997) Effect of bee pollen extract on glutathione system activity in mice liver under X-ray irradiation. *Ukrainskii Biokhimicheskii Zhurnal* 69 (4): 115-117.
14. BOGDANOV, S (2006) Contaminants of bee products. *Apidologie* 38 (1): 1-18.
15. BOGDANOV, S; BIERI, K; GREMAUD, G; IFF, D; KÄNZIG, A; SEILER, K; STÖCKLI, H; ZÜRCHER, K (2003) Bienenprodukte; 23 B Pollen. *Swiss Food Manual (Schweiz.Lebensmittelbuch)*: 1-6.
16. BOGDANOV, S; BIERI, K; GREMAUD, G; IFF, D; KÄNZIG, A; SEILER, K; STÖCKLI, H; ZÜRCHER, K (2004) Swiss Food Manual: Pollen *Bienenprodukte*, BAG (Swiss Federal Office for Public Health); Berne
17. BRUNETON, J (1999) *Pharmacognosie: Phytochimie, Plantes médicinales*. Lavoisier TEC DOC Paris (3rd. edition)

18. BUCK, A C; COX, R; REES, R W M (1990) Treatment of outflow tract obstruction due to benign prostatic hyperplasia with the pollen extract, Cernilton: a double-blind, placebo-controlled study. *British Journal of Urology* 66: 398-404.
19. BUCK, A C; REES, R W M; EBELING, L (1989) Treatment of chronic prostatitis and prostatodynia with pollen extract. *British Journal of Urology* 64: 496-499.
20. CAILLAS, A (1975) *The pollen*. Apimondia; 86 pp
21. CAMPOS, M (1997) Caracterização do pólen apícola pelo seu perfil em compostos fenólicos e pesquisa de algumas actividades biológicas. Faculty of Pharmacy, University of Coimbra Coimbra
22. CAMPOS, M; CUNHA, A; MARKHAM, K (1998) Inhibition of Virulence of *Pseudomonas aeruginosa* cultures, by flavonoids isolated from bee-pollen: possible structure-activity relationships. Polyphenol communications 98., XIX<sup>th</sup> international conference on polyphenols, Lille
23. CAMPOS, M; FRIGERIO, C; LOPES, J; BOGDANOV, S (2010) What is the future of Bee-Pollen? *JAAS* 2: 131-144.
24. CAMPOS, M; MARKHAM, K R; MITCHELL, K A; DA CUNHA, A P (1997) An approach to the characterization of bee pollens via their flavonoid/phenolic profiles. *Phytochemical Analysis* 8 (3): 181-185.
25. CAMPOS, M G; CUNHA, A; NAVARRO, M C; UTRILLA, M P (1994) Free radical scavenging activity of bee pollen. *Bull.Group.Polyphenols*. 17: 415-416.
26. CAMPOS, M G; WEBBY, R F; MARKHAM, K R; MITCHELL, K A; DA CUNHA, A P (2003) Age-Induced Diminution of free radical scavenging capacity in bee pollens and the contribution of Consistent flavonoids. *Journal of agricultural and food chemistry* 51 (3): 742-745.
27. CAMPOS, M G R; BOGDANOV, S; ALMEIDA-MURADIAN, L B; SZCZESNA, T; MANCEBO, Y; FRIGERIO, C; FERREIRA, F (2008) Pollen composition and standardisation of analytical methods. *Journal of Apicultural Research* 47 (2): 154-161.
28. CARPES, S T; BEGNINI, R; DE ALENCAR, S M; MASSON, M L (2007) Study of preparations of bee pollen extracts, antioxidant and antibacterial activity. *Ciencia e Agrotecnologia* 31 (6): 1818-1825.
29. CHAMBLISS, W (2003) A Critical Review of Graminex Flower pollen extract for Symptomatic Relief Of Lower Urinary Tract Symptoms (LUTS) in Men.: 4-9.
30. CHAUVIN, R (1968) Action physiologique et therapeutique des produits de la ruche *Traite de biologie de l'abeille*, Masson; Paris; pp 116-154.
31. CHAUVIN, R (1987) Le pollen *La ruche et l'homme*, Calmann-Lévy; pp 77-106.
32. CHOI, E (2007) Antinociceptive and Antiinflammatory Activities of Pine (*Pinus densiflora*) Pollen Extract. *Phytother.Res.* 21: 471-475.
33. CHOI, J H; JANG, Y S; OH, J W; KIM, C H; HYUN, I G (2015) Bee Pollen-Induced Anaphylaxis: A Case Report and Literature Review. *Allergy Asthma Immunol Res* 7: 513-517.
34. COHEN, S H; YUNGINGER, J W; ROSENBERG, N; FINK, J N (1979) Acute allergic reaction after composite pollen ingestion. *Journal of Allergy and Clinical Immunology* 64 (4): 270-274.
35. COOK, N; STAMPFER, M; MA, J; MANSON, J; SACKS, F; BURING, J; HENNEKENS, C (1999) Beta-carotene supplementation for patients with low baseline levels and decreased risks of total and prostate carcinoma. *Cancer* 86: 1629-1631.
36. CRANE, E (1999) History of other products from bees *The world history of beekeeping and honey hunting*, Gerald Duckworth & Co Ltd; London; pp 545-553.
37. CRISTEA, E; SOMMER, L; TRIFAN, C; TUDOR, N (1976) Antihepatotoxisches Präparat auf der Basis von Carduus-Extrakt und Pollen *Neues in der Apitherapie*, Apimondia; Bukarest; pp 285-289.

38. DE MELO PEREIRA, I (2008) Stability of antioxidant vitamins in bee pollen samples (original in Portuguese). PhD Pharmaceutical Science School Sao Paulo University, Sao Paulo, Brazil; pp 90pp.
39. DE MELO PEREIRA, I; ALMEIDA-MURADIAN, L (2010) Stability of antioxidant vitamins in bee pollen samples. *Quimica Nova* 33: 514-518.
40. DE OLIVEIRA, M C; DA SILVA, D M; LOCH, F C; MARTINS, P C; DIAS, D M B; SIMON, G A (2013) Effect of Bee Pollen on The Immunity and Tibia Characteristics in Broilers. *Brazilian Journal of Poultry Science* 15 (4): 323-327.
41. DOMINGUEZ-VALHONDO, D; GIL, D B; HERNANDEZ, M T; GONZALEZ-GOMEZ, D (2011) Influence of the commercial processing and floral origin on bioactive and nutritional properties of honeybee-collected pollen. *International Journal of Food Science and Technology* 46 (10): 2204-2211.
42. DONGA, J; GAO, K; WANGA, K; XUA, X; ZHANGA, H (2015) Cell Wall Disruption of Rape Bee Pollen Treated with Combination of Protamex Hydrolysis and Ultrasonication. *Food Research International* 75: 123-130.
43. DUBRISAY, J (1972) A new natural treatment for protein malnutrition states. Results of a double-blind clinical trial. *Gazette Medical de France* 79: 7674-7683.
44. DUBTSOVA, E; KOMISARENKO, I; KASSYANENKO, V (2007) Bee pollen and bee bread: biological action and use in aged people. *Clin Gerontol (Russia)* 13 (1): 50-52.
45. DUDOV, I A; MORENETS, A A; ARTYUKH, V P; STARODUB, N F (1994) Immunomodulatory effect of honeybee flower pollen load. *Ukrainskii Biokhimicheskii Zhurnal* 66 (6): 91-93.
46. DUDOV, I A; STARODUB, N F (1994) Antioxidant system of rat erythrocytes under conditions of prolonged intake honeybee flower pollen load. *Ukrainskii Biokhimicheskii Zhurnal* 66 (6): 94-96.
47. DUTAU, G; RANCE, F (2009) Honey and honey-product allergies. *Revue Francaise D Allergologie* 49 (6): S16-S22.
48. DUTKIEWICZ, S (1996) Usefulness of Cernilton in the treatment of benign prostatic hyperplasia. *International Urology and Nephrology* 28 (1): 49-53.
49. ELIST, J (2006) Effects of pollen extract preparation Prostat/Polit on lower urinary tract symptoms in patients with chronic nonbacterial prostatitis/chronic pelvic pain syndrome: a randomized, double-blind, placebo-controlled study. *Urology* 67: 60-63.
50. ERASLAN, G; KANBUR, M; SILICI, S (2008) Effect of carbaryl on some biochemical changes in rats: The ameliorative effect of bee pollen. *Food Chem Toxicol.*: in print.
51. ERASLAN, G; KANBUR, M; SILICI, S; LIMAN, B; ALTINORDULU, S; KARABACAK, M (2008) Evaluation of Protective Effect of Bee Pollen Against Propoxur Toxicity in Rat. *Ecotoxicology and Environmental Safety* doi:10.1016/j.ecoenv.2008.06.008 (5)
52. ERKMEN, O; OZCAN, M M (2008) Antimicrobial effects of Turkish propolis, pollen, and laurel on spoilage and pathogenic food-related microorganisms. *Journal of Medicinal Food* 11 (3): 587-592.
53. EUROPEAN PARLIAMENT AND COUNCIL (2007) REGULATION (EC) No 1924/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 20 December 2006 on nutrition and health claims made on foods. *Official Journal of the European Union* L 404: L 12-3-L 12/17.
54. FATRCOVA-SRAMKOVA, K; NOZKOVA, J; KACANIOVA, M; MARIASSYOVA, M; ROVNA, K; STRICIK, M (2013) Antioxidant and antimicrobial properties of monofloral bee pollen. *Journal of Environmental Science and Health Part B-Pesticides Food Contaminants and Agricultural Wastes* 48 (2): 133-138.
55. FIVEASH, J; MCCONNELL, J (1989) A Storage Method for Pollen Using Freeze Drying. *TreePlanters' Notes*: 18-19.
56. FRANCHI, G G; FRANCHI, G; CORTI; POMPELLA, A (1997) Microspectroscopic evaluation of digestibility of pollen grains. *Plant Foods for Human Nutrition* 50 (2): 115-126.

57. FRANCIS, J N; TILL, S J; DURHAM, S R (2003) Induction of IL-10(+)/CD4(+)/CD25(+) T cells by grass pollen immunotherapy. *Journal of Allergy and Clinical Immunology* 111 (6): 1255-1261.
58. FURUSAWA, E; CHOU, S C; HIRAZUMI, A; MELERA, A (1995) Antitumour potential of pollen extract on lewis lung carcinoma implanted intraperitoneally in syngeneic mice. *Phytotherapy Research* 9 (4): 255-259.
59. GEORGIJEWA, E; WASSILEFF, W (1993) Pollen against Anemia, 29 Apimondia Kongress in Budapest: pp 106.
60. GERGEN, I; RADU, F; BORDEAN, D; ISENGARD, H D (2006) Determination of water content in bee's pollen samples by Karl Fischer titration. *Food Control* 17 (3): 176-179.
61. GERGEN, I; RADU, F; POIANA, M (2005) Bee's pollen moisture determination by halogen lamp infrared drying method. *Revista de Chimie* 56 (1): 54-56.
62. GEYMAN, J P (1994) Anaphylactic reaction after ingestion of bee pollen. *The Journal of the American Board of Family Practice / American Board of Family Practice* 7 (3): 250-252.
63. GREENBERGER, P A; FLAIS, M J (2001) Bee pollen-induced anaphylactic reaction in an unknowingly sensitized subject. *Annals of allergy, asthma & immunology* 86 (2): 239-242.
64. HABIB, F K; ROSS, M; BUCK, A C (1990) In vitro evaluation of the pollen extract, Cernitin T-60, in the regulation of prostate cell growth. *British Journal of Urology* 66: 393-397.
65. HAMAMOTO, R; ISHIYAMA, K; HASHIMOTO, K; YAMAGUCHI, M (2006) Characterization of the active component in bee pollen *Cistus ladaniferus* extract in stimulating bone calcification and in inhibiting bone resorption in vitro. *Journal of Health Science* 52 (5): 607-612.
66. HAMAMOTO, R; ISHIYAMA, K; YAMAGUCHI, M (2006) Inhibitory effects of bee pollen *Cistus ladaniferus* extract on bone resorption in femoral tissues and osteoclast-like cell formation in bone marrow cells in vitro. *Journal of Health Science* 52 (3): 268-275.
67. HAN, X; SHEN, T; LOU, H. (2007) Dietary Polyphenols and Their Biological Significance. *Int.J.Mol.Sci.* 8: 950-988.
68. HARI, K; KESAVA, K; RAVIKUMAR, A; SUPRIYA, M; RAM, C; STANLEY, A (2004) Inhibition of prostate cancer cell colony formation by the flavonoid quercetin correlates with modulation of specific regulatory genes. *Clin Diag Lab Immunol* 11: 63-69.
69. HARO, A; LOPEZ-ALIAGA, I; LISBONA, F; BARRIONUEVO, M; ALFEREZ, M J M; CAMPOS, M S (2000) Beneficial effect of pollen and/or propolis on the metabolism of iron, calcium, phosphorus, and magnesium in rats with nutritional ferropenic anemia. *Journal of agricultural and food chemistry* 48 (11): 5715-5722.
70. HERBERT, E W, JR.; MILLER-IHLI, N J (1987) Seasonal variation of seven minerals in honey bee collected pollen. *American Bee Journal*: 367-369.
71. HERNUSS, P; MÜLLER-TYL, E; SALZER, H; SINZINGER, H; WICKE, L; PREY, T; REISINGER, L (1975) Pollendiät als Adjuvans der Strahlentherapie gynäkologischer Karzinome. *Strahlentherapie* 150 (5): 500-506.
72. HERNUSS, P; MÜLLER-TYL, E; SALZER, H; SINZINGER, H; WICKE, L; PREY, T; REISINGER, L (1975) Pollendiät als Adjuvans der Strahlentherapie gynäkologischer Karzinome. *Strahlentherapie* 150 (5): 500-506.
73. HODGES, D (1952) *The pollen loads of the honeybee*. Bee Research Association Limited London
74. IALOMITEANU, M; DAGHIE, V; NICOLAU, N; RADULESCU, M (1976) Behandlung von Hepatitiden mit Pollen und Bienenbrot *Neues in der Apitherapie*, Apimondia; Bukarest; pp 292-302.
75. ISHIKAWA, Y; TOKURA, T; NAKANO, N; HARA, M; NIYONSABA, F; USHIO, H; YAMAMOTO, Y; TADOKORO, T; OKUMURA, K; OGAWA, H (2008) Inhibitory Effect of Honeybee-Collected Pollen on Mast Cell Degranulation In Vivo and In Vitro. *Journal of Medicinal Food* 11: 14-20.

76. IVERSEN, T; FIIRGAARD, K M; SCHRIVER, P; RASMUSSEN, O; ANDREASEN, F (1997) The effect of NaO Li Su on memory functions and blood chemistry in elderly people. *Journal of Ethnopharmacology* 56 (2): 109-116.
77. IZUTA, H; SHIMAZAWA, M; TSURUMA, K; ARAKI, Y; MISHIMA, S; HARA, H (2009) Bee products prevent VEGF-induced angiogenesis in human umbilical vein endothelial cells. *BMC Complementary and Alternative Medicine* 9
78. JAGDIS, A; SUSSMAN, G (2012) Anaphylaxis from bee pollen supplement. *Canadian Medical Association Journal* 184 (10): 1167-1169.
79. JORDE, W; LINSKENS, H F (1974) Zur Persorption von Pollen und Sporen durch die intakte Darmschleimhaut. *Acta Allergologica* 29: 165-175.
80. JUZWIAK, S (1993) Experimental evaluation of the effect of pollen extract on the course of paracetamol poisoning (in Polish; English abstract). *Annales Academiae Medicae Stetinensis* 39: 57-69.
81. KACANIOVA, M; ROVNA, K; ARPASOVA, H; HLEBA, L; PETROVA, J; HASCIK, P; CUBON, J; PAVELKOVA, A; CHLEBO, R; BOBKOVA, A; STRICIK, M (2013) The effects of bee pollen extracts on the broiler chicken's gastrointestinal microflora. *Research in Veterinary Science* 95 (1): 34-37.
82. KAHLERT, H; STUWE, H T; CROMWELL, O; FIEBIG, H (1999) Reactivity of T cells with grass pollen allergen extract and allergoid. *International Archives of Allergy and Immunology* 120 (2): 146-157.
83. KASSYANENKO, V; KOMISARENKO, I; DUBTSOVA, E (2010) Influence of honey, pollen and bee bread on serum cholesterolin of patients with pathological lipid metabolism (Russian), *Beekeeping, apitherapy and life quality*, International Industrial Academy, Moscow, 20.May2010: pp 81-82.
84. KEDZIA, B (2008) Chemical composition and adaptogenic activity of honeybee collected pollen: part one: adaptogenic activity. *Postepi fitoterapii* 2: 115-124.
85. KEMPF, M; REINHARD, A; BEUERLE, T (2010) Pyrrolizidine alkaloids (PAs) in honey and pollen-legal regulation of PA levels in food and animal feed required. *Molecular Nutrition & Food Research* 54 (1): 158-168.
86. KHAN, N; AFAQ, F; MIKHTAR, H (2006) Apoptosis by dietary factors: the suicide solution for delaying cancer growth. *Carcinogenesis* 28: 233-239.
87. KHINCHI, M; POULSEN, L; CARAT, F; ANDRÉ, C; HANSEN, A; MALLING, H (2002) Clinical efficacy of sublingual and subcutaneous birch pollen allergen-specific immunotherapy: a randomized, placebo-controlled, double-blind, double-dummy stud. *Allergy* 59: 45-53.
88. KIM, L; RIEDLINGER; J. BALDWIN, C; HILLI, L; KHALSA, S; MESSER, S; WATERS, R (2005) Treatment of Seasonal Allergic Rhinitis Using Homeopathic Preparation of Common Allergens in the Southwest Region of the US: A Randomized, Controlled Clinical Trial. *Annals Pharmacother* 39: 617-624.
89. KIRK, W (1994) *A colour guide to pollen loads of honey bee*. International Bee Research Association Cardiff
90. KLIPPEL, K; HILTL, D; SCHIPP, B (2003) A multicentric, placebo-controlled, double-blind clinical trial of &beta;-sitosterol (phytosterol) for the treatment of benign prostatic hyperplasia. *Brit J Urol* 3: 427-432.
91. KOC, A N; SILICI, S; KASAP, F; HORMET-OZ, H T; MAVUS-BULDU, H; ERCAL, B D (2011) Antifungal Activity of the Honeybee Products Against *Candida* spp. and *Trichosporon* spp. *J. Med. Food* (7): 1-7.
92. KOLESAROVA, A; BAKOVA, Z; CAPCAROVA, M; GALIK, B; JURACEK, M; SIMKO, M; TOMAN, R; SIROTKIN, A V (2013) Consumption of bee pollen affects rat ovarian functions. *Journal of Animal Physiology and Animal Nutrition* 97 (6): 1059-1065.
93. KOSLIK, S; TAKAC, M (1979) Beeinflussung der Hypertriglyzeridämie und Urikämie von dauerdialysebehandelten Patienten durch Pollen. *Das Deutsche Gesundheitswesen* 34 (38): 1850-1853.
94. KOSMIDER, K; WOJCICKI, J; SAMOCHOWIEC, L; WOYKE, M; GORNIK, W (1983) Effect of cernilton on platelet aggregation in vivo. *Herba Polonica* 29: 237.

95. KRELL, R (1996) *Value-added products from beekeeping*. FAO Food and Agriculture Organization of the United Nations Roma; 409 pp
96. KROYER, G; HEGEDUS, N (2001) Evaluation of bioactive properties of pollen extracts as functional dietary food supplement. *Innovative Food Science & Emerging Technologies* 2 (3): 171-174.
97. LARSEN TH; POULSEN LK; MELAC M; COMBEBIAS A; ANDRE C; MALLING HJ (2006) Safety and tolerability of grass pollen tablets in sublingual immunotherapy – a phase-1 study. *Allergy* 61: 1173-1176.
98. LE BLANCA, B; DAVIS, O; BOUE, S; DE LUCCA, A; DEEBYA, T (2009) Antioxidant Activity of Sonoran Desert Bee Pollen. *Food Chem* doi:10.1016/j.foodchem.2009.01.055
99. LEJA, M; MARECZEK, A; WYZGOLIK, G; KLEPACZ-BANIAK, J; CZEKONSKA, K (2007) Antioxidative properties of bee pollen in selected plant species. *Food Chemistry* 100 (1): 237-240.
100. LEONAWITSCHJUS, R P (1976) Behandlung hypochromer Anämie mit Bienenbrot *Neues in der Apitherapie*, Apimondia; pp 93-96.
101. LEPARQ, G (1973) A new appetite stimulant drug based on pollen extracts with no hormonal or antihistamine action, in pediatric practice. Report of 100 cases. *La vie Medicale* 54: 1352-1354.
102. LEPLEY, D M; LI, B; BIRT, D F; PELLING, J C (2008) The chemopreventive flavonoid apigenin induces G<sub>2</sub>/M arrest in keratinocytes. *Carcinogene* 17: 2367-2375.
103. LIFTEROVR; FOMIN, W; SHISHKINA, L; AGAFONOVA, W; SOLDATOV, E G E; MARHOVSKAYA I.; PUSHKAREVA, S (2009) Experience with the use of bee bread for the treatment of dislipidemia of patients with high or intermediate risk for heart disease having arterial hypertension, *Apitherapy today (in Russian)*, Ribnoe: pp 54-55.
104. LIN, X L; ZHU, L Q; LI, L M (1990) Morphological changes in aged canine prostatic hyperplasia treated with bee pollen. *Chin Tradit Herb Drugs* 21: 164-166.
105. LINSKENS, H F; JORDE, W (1997) Pollen as food and medicine - A review. *Economic Botany* 51 (1): 78-86.
106. LIU, X L; LI, L M (1990) Morphological observation of effect of bee pollen on intercellular lipofuscin in NIH mice. *J Chin Mater Med Zhongguo Zhongyao Zazhi* 15: 561-563.
107. LOUVEAUX, J; MAURIZIO, A; VORWOHL, G (1978) Methods of melissopalynology. *Bee World* 59 (4): 139-162.
108. MANNING, R (2001) Fatty acids in pollen: a review of their importance for honey bees. *Bee World* 82 (2): 60-75.
109. MARGHITAS, L; STANCIU, O; DEZMIREAN, D; BOBIS, O; POPESCU, O; BOGDANOV, S; CAMPOS, M (2009) In vitro antioxidant capacity of honeybee-collected pollen of selected floral origin harvested from Romania. *Food.Chem.* doi:10.1016/j.foodchem.2009.01.014
110. MARUYAMA, H; SAKAMOTO, T; ARAKI, Y; HARA, H (2010) Anti-inflammatory effect of bee pollen ethanol extract from *Cistus* sp of Spanish on carrageenan-induced rat hind paw edema. *BMC Complementary and Alternative Medicine* 10
111. MAUGHAN, R J; EVANS, S P (1982) Effects of pollen extract upon adolescent swimmers. *British Journal of Sports Medicine* 16 (3): 142-145.
112. MEDEIROS, K C P; FIGUEIREDO, C A V; FIGUEREDO, T B; FREIRE, K R L; SANTOS, F A R; ALCANTARA-NEVES, N M; SILVA, T M S; PIUVEZAM, M R (2008) Anti-allergic effect of bee pollen phenolic extract and myricetin in ovalbumin-sensitized mice. *Journal of Ethnopharmacology* 119 (1): 41-46.
113. MOINGEON, P; HRABINAA, M; BERGMANN, K; JAEGERD, S; FRATIE, F; BORDASA, V; PELTREB, G (2008) Specific Immunotherapy for Common Grass Pollen Allergies: Pertinence of a Five Grass Pollen Vaccine. *Int Arch Allergy Immunol* 146: 338-342.
114. MOOSBECKHOFER, R; ULZ, J (1996) *Der erfolgreiche Imker*. Graz-Stuttgart

115. MORGANO, M A; TEIXEIRA MARTINS, M C; RABONATO, L C; MILANI, R F; YOTSUYANAGI, K; RODRIGUEZ-AMAYA, D B (2012) A Comprehensive Investigation of the Mineral Composition of Brazilian Bee Pollen: Geographic and Seasonal Variations and Contribution to Human Diet. *Journal of the Brazilian Chemical Society* 23 (4): 727-736.
116. MURAKAMI, M; TSUKADA, O; OKIHARA, K; HASHIMOTO, K; YAMADA, H; YAMAGUCHI, H (2008) Beneficial effect of honeybee-collected pollen lump extract on benign prostatic hyperplasia (BPH) - A double-blind, placebo-controlled clinical trial - 102. *Food Science and Technology Research* 14 (3): 306-310.
117. MURRAY, F (1991) Get the buzz on bee pollen. *Better Nutr.* 31: 20-21.
118. NABAVI, S E A (2015) Neuroprotective effects of chrysin: From chemistry to medicine. *Neurochemistry International* 90: 224-231.
119. NAGAI, T; INOUE, R; INOUE, H; SUZUKI, N (2002) Scavenging capacities of pollen extracts from *Cistus ladaniferus* on autoxidation, superoxide radicals, hydroxyl radicals, and DPPH radicals. *Nutrition-Research New York* 22 (4): 519-526.
120. NAGAI, T; INOUE, R; SUZUKI, N; TANOUE, Y; KAI, N; NAGASHIMA, T (2007) Antihypertensive activities of enzymatic hydrolysates from honeybee-collected pollen of *Cistus ladaniferus* 212. *Journal of Food Agriculture & Environment* 5 (3-4): 86-89.
121. NAGAI, T; NAGASHIMA, T; MYODA, T; INOUE, R (2004) Preparation and functional properties of extracts from bee bread 79. *NAHRUNG FOOD* 48 (3): 226-229.
122. NAGASHIMA, A; ISHII, M; YOUSHINAGA, M; HIGAKI, E (1998) Effect of Cernitin™ pollen-extract (Cernilton®) on the Function of Urinary Bladder in Conscious Rats. *Jpn Pharmacol Ther* 26 (11)
123. NAIR, H; RAO, K; AALINKEEL, R; MAHAJAN, S; CHAWDA, R; AND SCHWARTZ, S (2004) Inhibition of Prostate Cancer Cell Colony Formation by the Flavonoid Quercetin Correlates with Modulation of Specific Regulatory Genes. *Clin Diagn Lab Immun* 11: 63-69.
124. NAKASE K; KIMURA I; KIMURA M. (1990) Effects of Pollen-Extract Components, Diamines and Derivatives of Feruloylputrescine on Isolated Bladder and Urethral Smooth Muscles of Mice. *Jpn J Pharmacol.* 53: 157-164.
125. NECHAEVA, N (2009) Changes of functional and sport medicine after intake of bee products. Ryazan State Medical University Ryazan; pp 1-250.
126. NOURI-ARIA, K T; WACHHOLZ, P A; FRANCIS, J N; JACOBSON, M R; WALKER, S M; WILCOCK, L K; STAPLE, S Q; AALBERSE, R C; TILL, S J; DURHAM, S R (2004) Grass pollen immunotherapy induces mucosal and peripheral IL-10 responses and blocking IgG activity. *Journal of Immunology* 172 (5): 3252-3259.
127. OLIVEIRA, K (2006) Caracterização do pólen apícola e utilização de vitaminas antioxidantes como indicadores do processo de desidratação. University of Sao Paolo Sao Paolo, Brazil
128. OZCAN, M (2004) Inhibition of *Aspergillus parasiticus* NRRL 2999 by pollen and propolis extracts. *Journal of Medicinal Food* 7 (1): 114-116.
129. ÖZCAN, M; CEYLAN, D A; ÜNVER, A; YETISIR, R (2003) Antifungal effect of pollen and propolis extracts collected from different regions of Turkey 1132. *Uludag Bee Journal* 3 (3): 27-34.
130. PELLEGRINI, N; SERAFINI, M; COLOMBI, B; DEL RIO, D; SALVATORE, S; BIANCHI, M; BRIGHENTI, F (2003) Total Antioxidant Capacity of Plant Foods, Beverages and Oils Consumed in Italy Assessed by Three Different In Vitro Assays. *J. Nutrition* 133: 2812-2819.
131. PENG, HF; XUE, Z; MIAO, F; PAN, D; LIU, Z; LIU, Z; LIU, S; TAO, S (1990) The effect of pollen in enhancing tolerance to hypoxia and promoting adaptation to highlands. *Zhonghua Yi Xue Za Zhi* 70: 77-81.

132. PERCIE DU SERT, P (2002) *Ces pollens qui nous soignent*. Paris; 211 pp (Guy Trédaniel. edition)
133. PERCIE DU SERT, P (2009) Les pollens apicoles. *Phytotherapie* 7: 75-82.
134. PERCIE DU SERT, P (2009) Probiotic effect of lactic acid bacteria in fresh pollen, *41st Apimondia Congress Montpellier*
135. PHAM-HUY, L; HE, H; PHAM-HUY, C (2008) Free Radicals, Antioxidants in Disease and Health. *Int.J.Biomed.Sci.* 4: 89-96.
136. PICHICHERO, E; CICCONI, R; MATTEI, M; CANINI, A (2010) Chrysin-induced apoptosis is mediated through p38 and Bax activation in B16-F1 and A375 melanoma cells. *International Journal of Oncology* Doi: 10.3892/ijo.2010.876: 473-483.
137. PINTO, B; CACIAGLI, F; RICCIO, E; REALI, D; SARIC, A; BALOG, T; LIKIC, S; SCARPATO, R (2010) Antiestrogenic and antigenotoxic activity of bee pollen from *Cystus incanus* and *Salix alba* as evaluated by the yeast estrogen screen and the micronucleus assay in human lymphocytes. *European journal of medicinal chemistry* 45 (9): 4122-4128.
138. PUENTE, S; INIGUEZ, A; SUBIRATS, M; ALONSO, M J; POLO, F; MONEO, I (1997) Eosinophilic gastroenteritis caused by bee pollen sensitization. *Medicina clínica* 108 (18): 698-700.
139. PUNYAKIN, A (2001) Biochemical evaluation of the use of bee products in sport medicine (in Russian). University of Ryazan Ryazan; pp 1-136.
140. QIAN, B C; ; ZANG, X; QI, B; MAO, L; XI, Y (1987) Immunoenhancement activity of bee pollen and its acetone extract in mice. *Acta Nutrimenta Sinica* 3 (3)
141. QIAN, B C; ZANG, X X; LIU, X L (1990) Effects of bee-collected pollen on lipid peroxides and immune response in aging and malnourished mice. *Chinese Materia Medica* 15: 301-303.
142. RABIE, A L; WELLS, J D; DENT, L K (1983) The nitrogen content of pollen protein. *Journal of Apicultural Research* 22 (2): 119-123.
143. REBIEN, W; PUTTONEN, E; MAASCH, H; STIX, E; WAHN, U (1982) Clinical and immunological response to oral and subcutaneous immunotherapy with grass pollen. *European journal of pediatrics* 138: 341-344.
144. REISNER, W; GARTLEHNER, K (2006) Entwicklung einer maschinentauglichen Identifikationsmethode für Blütenpollen. *Berichte aus Energie und Umweltforschung* 24: 1-36.
145. RIMPLER, M (2003) Von Bienen gesammelte Blütenpollen: Eigenschaften und Verwendung. *Ärztzeitschrift für Naturheilverfahren* 44 (3): 158-165.
146. ROULSTON, T H; CANE, J H (2000) Pollen nutritional content and digestibility for animals. *Plant Systematics and Evolution* 222 (1-4): 187-209.
147. RUGENDORFF, E W; WEIDNER, W; EBELING, L; BUCK, A C (1993) Results of treatment with pollen extracts (Cernilton N) in chronic prostatitis and prostatodynia. *British Journal of Urology* 71: 433-438.
148. RZEPECKA-STOJKO A; STOJKO, J; KUREK-GÓRECKA, A; GÓRECKI, M; KABALA-DZIK, A; KUBINA, R; MOZDZIERZ, A; BUSZMAN, E (2015) Polyphenols from Bee Pollen: Structure, Absorption, Metabolism and Biological Activity. *Molecules* doi:10.3390/molecules201219800
149. RZEPECKA-STOJKO, A; PILAWA, B; RAMOS, P; STOJKO, J (2012) Antioxidative Properties of Bee Pollen Extracts Examined by Epr Spectroscopy. *Journal of Apicultural Science* 56 (1): 23-31.
150. RZEPECKA-STOJKO, A; STEC, M; KURZEJA, E; GAWRONSKA, E; PAWLOWSKA-GORAL, K (2012) The Effect of Storage of Bee Pollen Extracts on Polyphenol Content. *Polish Journal of Environmental Studies* 21 (4): 1007-1011.
151. SADEN-KREHULA, M; TAJIC, M (1987) Vitamin D and its metabolites in the pollen of pine. Part 5: Steroid hormones in the pollen of pine species. *Pharmazie* 42: 471-472.

152. SAMOCHOWIEC, L; WOJCICKI, J (1981) Effect of pollen on serum and liver lipids in rats fed on a high-lipid diet. *Herba Polonica* 27 (4): 333-339.
153. SARIC, A; BALOG, T; SOBOCANEC, S; KUSIC, B; SVERKO, V; RUSAK, G; LIKIC, S; BUBALO, D; PINTO, B; REALI, D; MAROTTI, T (2009) Antioxidant effects of flavonoid from Croatian *Cystus incanus* L. rich bee pollen. *Food and Chemical Toxicology* 47 (3): 547-554.
154. SAWIKR, Y E AL (2017) Neuroinflammation in Alzheimer's Disease: The Preventive and Therapeutic Potential of Polyphenolic Nutraceuticals. *Advances in Protein Chemistry and Structural Biology* 108: 33-57.
155. SCHMIDT, J O; SCHMIDT, P J (1984) Pollen digestability and its potential nutritional value. *Gleanings in Bee Culture*: 320-322.
156. SERRA BONVEHI, J; GOMEZ PAJUELO, A (1987) Etude de la conservation du pollen des abeilles, emploi de fumigants. *Def.Vegetaux* 243: 90-94.
157. SERRA BONVEHI, J; GONELL GALINDO, J; GOMEZ PAJUELO, A (1986) Estudio de la composicion y características fisico-químicas del polen de abejas. *Alimentaria*: 63-67.
158. SERRA BONVEHI, J; MARTI CASANOVA, T (1987) Estudio analítico para determinar la humedad del polen. Analytical study of quantification of moisture in pollen. *Anales de Bromatologia* 39: 339-349.
159. SERRA, B J; SOLIVA, T M; CENTELLES, L E (2001) Evaluation of polyphenolic and flavonoid compounds in honeybee-collected pollen produced in Spain. *Journal of agricultural and food chemistry* 49 (4): 1848-1853.
160. SHKENDEROV, S; IVANOV, T (1983) Pcelni Produkti, The Bee Products (in Bulgarian). *Zemizdat (Abstract in Honey bibliography)*: 1-238.
161. SHOSKES, D A (2002) Phytotherapy in chronic prostatitis. *Urology* 60 (6 Suppl): 35-37.
162. SIMOPOULOS, A (1991) Omega-3 fatty acids in health and disease and in growth and development. *AJCN* 54: 438-463.
163. SLIJEPCEVIC, M; NADZIJA, M; BLAZI-POLJAK, M; BORANIC, M (1978) Impact of the pollen contained in food on the reproduction of mice *IIIème Symposium international d'apithérapie*, Apimondia; Bukarest; pp 251-253.
164. SMIRNOVA, V (2008) Allergy towards bee products (in Russian), *Apitherapy today*, Ribnoe, 13.Oct.2008: pp 77-81.
165. SOARES DE ARRUDA, V A; SANTOS PEREIRA, A A; DE FREITAS, A S; BARTH, O M; DE ALMEIDA-MURADIAN, L B (2013) Dried bee pollen: B complex vitamins, physicochemical and botanical composition. *Journal of Food Composition and Analysis* 29 (2): 100-105.
166. SOLOMKA, V (2001) On bees pollen storage technologies. *Pasika* (3): 22-23.
167. SOMERVILLE, D C; NICOL, H I (2002) Mineral content of honeybee-collected pollen from southern New South Wales. *Australian Journal of Experimental Agriculture* 42 (8): 1131-1136.
168. STANLEY, R G; LINSKENS, H F (1974) *Pollen. Biology - Biochemistry - Management*. Springer-Verlag Berlin, Heidelberg
169. SZCZESNA, T (2006) Long chain fatty acids composition of of honeybee-collected pollen. *Journal of Apicultural Science* 50 (2): 65-79.
170. SZCZESNA, T (2006) Long-chain fatty acids composition of honeybee-collected pollen. *Journal of Apicultural Science* 50 (2): 65-79.
171. SZCZESNA, T; RYBAK, H; SKOWRONEK, W (1995) Alterations in the chemical composition of the pollen loads stored under various conditions: I, III, IV. *Pszczelnicze Zeszyty Naukowe* 40: 145, 171, 191-156, 189, 207.

172. TAYLOR, M; REILLY, D; LLEWELLYN, R; MCSHARRY, C; AITCHISON, T (2000) Treatment of Seasonal Allergic Rhinitis Using Homeopathic Preparation of Common Allergens in the Southwest Region of the US: A Randomized, Controlled Clinical Trial. *BMJ* 321: 471-476.
173. THOMPSON, I (2001) Pharmacologic agents in complementary medicine in prostatic disease. *Drugs of today* 37: 427-433.
174. TICHY, J; NOVAK, J (2000) Detection of antimicrobials in bee products with activity against viridans streptococci. *Journal of Alternative and Complementary Medicine* 6 (5): 383-389.
175. TIKHONOV, A I; SODSAVICHNIY, K; TICHONOV, C A; YARNICH, T G; BODNARCHUK, L I; KOTENKO, A M (2006) *Bee Pollen in Pharmacy and Medicine (in Russian)*. NFU Original Harkov
176. TIKHONOV, A I; SODZAVICHNIY, K; TIKHONOVA, S; YARNYH, T G; BODNARCHUK, L; KOTENKO, A (2006) *Flower pollen in pharmacy and medicine (monography in Russian)*. Orginal Kharkov, Ukraine
177. TRAILD-HOFFMANN, C; KASCHE, A; MENZEL, A; JAKOB, T; THIEL, M; RING, J; BEHRENDT, H (2003) Impact of pollen on human health : more than allergen carriers ? *International Archives of Allergy and Immunology* 131: 1-13.
178. TRAUTWEIN, E; DEMONTY, I (2007) Phytosterols: natural compounds with established and emerging health benefits. *Oléagineux, Corps Gras, Lipides* 14, 10.1684/ocl.2007.0145: 259-266.
179. TURNER, K K; NIELSEN, B D; O'CONNOR, C I; BURTON, J L (2006) Bee pollen product supplementation to horses in training seems to improve feed intake: a pilot study. *Journal of Animal Physiology and Animal Nutrition* 90 (9-10): 414-420.
180. ULBRICHT, C; CONQUER, J, G N; KHALSA, K; SKLAR, J; WEISSNER, W; WOODS, J (2009) An Evidence-Based Systematic Review of Bee Pollen by the Natural Standard Research Collaboration. *J.Dieth.Suppl.* 6: 290-312.
181. UZBEKOVA, D G; MAKAROVA, V; CHUGUNOVA, L; CHERNOBAVSKAYA, N; MIRGORODSKAYA, L (2001) Bee-collected pollen and lactulose in treatment of chronic hepatitis B in children. *Journal of Hepatology* 34: 194.
182. UZBEKOVA, D G; MAKAROVA, V; KHVOYNITSKAYA, L G; SLEPNEV, A A (2003) Evaluation of bee-collected pollen influence on lipid peroxidation, antioxidant system and liver function in old animals. *Journal of Hepatology* 38: 203.
183. VÁSQUEZ, A; OLOFSSON, T C (2009) The lactic acid bacteria involved in the production of bee pollen and bee bread. *Journal of apicultural research*, 48: 189-195.
184. WACHHOLZ, P A; SONI, N K; TILL, S J; DURHAM, S R (2003) Inhibition of allergen-IgE binding to B cells by IgG antibodies after grass pollen immunotherapy. *Journal of Allergy and Clinical Immunology* 112 (5): 915-922.
185. WANG, B; DIAO, Q; ZHANG, Z; LIU, Y; GAO, Q; ZHOU, Y; LI, S (2013) Antitumor activity of bee pollen polysaccharides from *Rosa rugosa*. *Molecular Medicine Reports* 7 (5): 1555-1558.
186. WANG, J; LI, S H; WANG, Q F; XIN, B Z; WANG, H (2007) Trophic effect of bee pollen on small intestine in broiler chickens. *Journal of Medicinal Food* 10 (2): 276-280.
187. WANG, J E A (2016) Neuroprotective Effect of Several Phytochemicals and Its Potential Application in the Prevention of Neurodegenerative Diseases. *Geriatrics* 1: 29.
188. WANG, M S; FAN, H F; XU, H J (1993) Effects of bee pollen on blood and hemopoietic system in mice and rats. *Chin Tradit Herb Drugs* 24: 588-591,601.
189. WOJCICKI, J; KOSMIDER, K; SAMOCHOWIEC, L; WOYKE, M (1983) Clinical evaluation of cernilton as lipidlowering agent. *Herba Polonica* 29: 55.

190. WOJCICKI, J; SAMOCHOWIEC, L (1984) Further studies in cernitins: screening of the hypolipidemic activity in rats. *Herba Polonica* 30: 115.
191. WOJCICKI, J; SAMOCHOWIEC, L; BARTLOMOWICZ, B; HINEK, A; JAWORSKA, M; GAWRONSKA-SZKLARZ, B (1986) Effect of atherosclerosis in rabbits. *Atherosclerosis Supplements* 62: 39.
192. WOODHOUSE, M; WILLIAMS, M; JACKSON, C (1987) The effects of varying doses of orally ingested bee pollen extract upon selected performance variables'. *Athletic Training* 22: 26-28.
193. WORTMANN, F (1977) Oral hyposensitization of children with pollinosis or house-dust asthma. *Allergol.Immunopathol.* 5 (3): 15-26.
194. WU, Y D; LOU, Y J (2007) A steroid fraction of chloroform extract from bee pollen of *Brassica campestris* induces apoptosis in human prostate cancer PC-3 cells  
194. *Phytotherapy Research* 21 (11): 1087-1091.
195. XIE YOU MEL; WAN BAOLIN; LI WEIMIN (1994) Effect of bee pollen on maternal nutrition and fetal growth. *Hua Xi Yi Ke Da Xue Xue Bao (chinese)* 25 (4): 434-437.
196. XUE, X; ZHAO, J; CHEN, L; ZHOU, J; YUE, B; LI, Y; WU, L; LIU, F (2012) Analysis of coenzyme Q10 in bee pollen using online cleanup by accelerated solvent extraction and high performance liquid chromatography. *Food Chemistry* 133 (2): 573-578.
197. YAKUSHEVA, E (2010) Pollen and bee bread: physico-chemical properties. Biological and pharmacological effects. Use in medical practice, In Rakita, D; Krivtsov, N; Uzbekova, D G (eds) *Theoretical and practical basics of apitherapy (Russian)*, Roszdrav; Ryazan; pp 84-97.
198. YAMAGUCHI, M; HAMAMOTO, R; UCHIYAMA, S; ISHIYAMA, K; HASHIMOTO, K (2006) Anabolic effects of bee pollen *Cistus ladaniferus* extract on bone components in the femoral-diaphyseal and -metaphyseal tissues of rats in vitro and in vivo. *Journal of Health Science* 52 (1): 43-49.
199. YAMAGUCHI, M; HAMAMOTO, R; UCHIYAMA, S; ISHIYAMA, K; HASHIMOTO, K (2007) Preventive effects of bee pollen *Cistus ladaniferus* extract on bone loss in streptozotocin-diabetic rats in vivo. *Journal of Health Science* 53 (2): 190-195.
200. YASUMOTO R.; KAWANISHI H.; TSUJINOT.; TSUJITA M.; NISHISAKA N.; HORII A.; KISHIMOTO, T (1995) Clinical evaluation of long term treatment using cernitin pollen extract in patients with benign prostatic hyperplasia. *Clin Ther* 17: 82-87.
201. YILDIZ, O; CAN, Z; SARAL, O; YULUG, E; OZTURK, F; ALIYAZICIOGLU, R; CANPOLAT, S; KOLAYLI, S (2013) Hepatoprotective Potential of Chestnut Bee Pollen on Carbon Tetrachloride-Induced Hepatic Damages in Rats. *Evidence-based complementary and alternative medicine*
202. YILDIZ, O; KARAHALIL, F; CAN, Z; SAHIN, H; KOLAYLI, S (2014) Total monoamine oxidase (MAO) inhibition by chestnut honey, pollen and propolis. *Journal of Enzyme Inhibition and Medicinal Chemistry* 29 (5): 690-694.
203. YOON, H-S; LIM, S-I; BYUN, M-W (1998) Changes in microbiological and physiochemical properties of bee pollen by application of gamma irradiation and ozone treatment. *Journal of Food Protection* 61 (2): 217-220.
204. ZENG, Z; WANG, L; RAO, B; FAN, Z; XIE, G (2004) A Study on the Effect of Honeybee Pollen Polysaccharide on Decreasing Lipoidemia in Rat. *Acta Agr.Univers.Jiangsiansis* 3
205. ZHANG, X; HABIB, F K; ROSS, M; BURGER, U; LEWINSTEIN, A; ROSE, K; JATON, J C (1995) Isolation and characterization of a cyclic hydroxamic acid from a pollen extract, which inhibits cancerous cell growth in vitro. *Journal of Medicinal Chemistry* 38 (4): 735-738.