

HEALTH-PROMOTING EFFECTS OF MANUKA HONEY

PROZDROWOTNE DZIAŁANIE MIODU MANUKA

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Summary

Honey properties are determined by the level of methylglyoxal (antimicrobial substance) from 30 to 550 in the case of MGO method or from 5 to 20 by UMF method. Previous studies have shown that high levels of methylglyoxal in Manuka honey support the body's defense mechanisms, mainly by stimulating the growth of probiotic intestinal bacteria. The antibacterial properties of honey make it possible to use it to treat wounds and bedsores and prevent inflammation in the body, which is important in a sports training.

The most significant study results showed that honey has a positive effect on increasing the body's immune response as it is highly antioxidant and anti-inflammatory. It means it can be used in healing wounds by stopping the growth of harmful bacteria, for example: *Staphylococcus aureus*. Its intake prevents the atherosclerosis. Moreover, acetylcholine present in Manuka honey lowers blood pressure and improves blood circulation, choline has a protective effect on the liver and increases the secretion of bile. Metal ions stimulate the production of red blood cells and hemoglobin. The high content of methylglyoxal, and thus, the specific health benefits of Manuka honey can be used in the diet and supplementation of athletes.

Changes occurring in the body due to physical exercise, like the oxidative stress, increase the level of free radicals, and in result, cause a fall in the exercise potential of the body as well as reduce the immunological barrier. This problem can be particularly observed in winter athletes. Current research results on pro-health properties of Manuka honey have indicated that it can counteract those negative effects. Namely, negative factors of physical exercise are blocked in an athlete's body by honey [1], and Manuka honey may, in particular, have a positive impact on the health of physically active people.

Keywords: methylglyoxal, honey, manuka, anti-inflammatory substances

Streszczenie

Miód pszczeli znany jest od wieków jako produkt spożywczy korzystnie oddziaływujący na organizm człowieka. W zależności od stężenia metyloglioksalu (substancji przeciwbakteryjnej) miody oznaczane są wartościami od 30 do 550 w przypadku metody MGO lub od 5 do 20 przy metodzie UMF. Dotychczasowe badania wykazały, że wysokie stężenie metyloglioksalu w miodach Manuka wspiera mechanizmy obronne organizmu m.in. poprzez pobudzanie wzrostu liczby probiotycznych bakterii jelitowych. Właściwości antybakteryjne miodu pozwalają na wykorzystanie go w leczeniu ran i odleżyn oraz przeciwdziałają stanom zapalnym w organizmie, co jest istotne w treningu sportowym.

Najważniejsze wyniki badań wykazały, że miód pozytywnie wpływa na zwiększenie odpowiedzi immunologicznej organizmu, działanie antyoksydacyjne i przeciwzapalne, leczenie ran i zatrzymanie rozwoju szkodliwych bakterii, jak np. gronkowiec złocisty. Jego spożywanie zapobiega zmianom miażdżycowym. Obecna w miodzie acetylocholina obniża ciśnienie i poprawia krążenie krwi, cholina działa ochronnie na wątrobę oraz zwiększa wydzielanie żółci. Jony metali stymulują produkcję czerwonych ciałek krwi i hemoglobiny. Wysoka zawartość metyloglioksalu i co za tym idzie, szczególne właściwości prozdrowotne miodu Manuka, mogą być wykorzystywane w diecie i suplementacji u sportowców.

Zmiany zachodzące w organizmie pod wpływem wysiłku fizycznego, min. zjawisko stresu oksydacyjnego, zwiększenie ilości wolnych rodników powodują obniżenie możliwości wysiłkowych organizmu i zmniejszenie bariery immunologicznej, na którą szczególnie narażeni są sportowcy zimowi. Negatywnym skutkiem może przeciwdziałać suplementacja miodem Manuka, na co wskazywać mogłyby dotychczasowe wyniki badań nad właściwościami prozdrowotnymi tej substancji. Negatywne czynniki są blokowane w organizmie sportowca przez miód (Davis, Perez 2009), ale miód Manuka może w szczególności pozytywnie oddziaływać na stan zdrowia osób aktywnych fizycznie.

Poniższa praca ma na celu przedstawienie prozdrowotnych właściwości miodu Manuka.

Słowa kluczowe: metyloglioksal, miód, Manuka, substancje przeciwzapalne

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Introduction

Manuka Honey is a natural product produced by bees from the nectar bush scoparium *Leptospermum* (Manuka bush). It grows mainly on the eastern shores of the islands of New Zealand and in the south-east. Australia. Manuka bush name is derived from the Maori language, inhabiting New Zealand, which used the healing properties of honey. Honey is beneficial for: heart and circulatory system (easy absorption of sugars does not burden the working of the heart), regulation of the heart rate (the presence of acetylcholine, potassium), hypotension (presence of acetylcholine), respiratory diseases (expectorant, coating mucous membranes, strengthening), detoxification of the body (binding toxic glucose), increase in bile (choline), lowering the level of lipids in the liver (choline), removing the swelling of vascular and cardiac nature (low protein content, sodium ion and chloride), stimulation of intestine peristalsis (large amount of fructose and choline), the regeneration of the mucosa of the stomach and duodenum (the presence of fructose), the metabolism of carbohydrates (acetylcholine), treatment of bedsores and tumor wounds (derived from fructose), inhibition of streptococcal - caries (hydrogen peroxide) [2].

The active ingredient in manuka honey is methylglyoxal, which has been explored by prof. Thomas Henle [3]. His analysis showed a relationship between the level of methylglyoxal in manuka honey and its effect on the antimicrobial activity [4]. Apart from methylglyoxal, honey consists of carbohydrates. The dominant one is maltose (19.6%), then isomaltose (15.5%) and sucrose (15.4%). The glucose level is low, at 11.6% and 4.3% fructose [5]. When comparing Manuka with Polish honeys one can notice the difference in the content of each carbohydrate, e.g. glucose, fructose, sucrose, and maltose. Native honeys contain 32% glucose and fructose at 38%. The content of maltose in Polish honey is approx. 3%, and sucrose approx. 2%.

Manuka honey has much higher antioxidant properties compared to other honeys [6]. Similar observations were also made comparing these honeys with European ones. Honey in Europe produced by *Apis mellifera* were characterized by significantly lower antioxidant activity compared to Manuka honey from *Leptospermum* species from New Zealand.

The noticeable difference in antioxidant and anti-inflammatory activity of Manuka honey distinguishes it from other bee products. In addition, it becomes an extremely interesting and valuable substance which use in sports nutrition and supplementation may be of great importance in the regeneration and good health of the athlete.

Aim of the work

The most significant study results showed that honey has a positive effect on increasing the body's immune response as it is highly antioxidant and anti-inflammatory. It means it can be used in healing wounds by stopping the growth of harmful bacteria. The high content of methylglyoxal, and thus, the specific health benefits of Manuka honey can be used in the diet and supplementation of athletes. This work aims to present health properties of Manuka honey for this group.

Brief description of the status of knowledge

Active Manuka honey compound

Methylglyoxal (propionaldehyde) is an antibacterial compound characteristic of manuka honey [3]. It is formed as an offshoot of the non-enzymatic conversion of dihydroxyacetone, present in variable amounts in the nectar of the Manuka flowers [7]. Studies have shown that the content of methylglyoxal in Manuka honey ranges from 38 to 761 mg / kg. For most honey samples from local shops the value does not exceed 3.1 mg / kg [4].

Henle'y et al [3] shown that the distinguishing activity of Manuka honey is due to the high levels of methylglyoxal, and not, as previously thought the presence of hydrogen peroxide, which is the most affecting inhibitor in traditional honeys [4]. The study sample involving the so-called catalase showed that the antimicrobial activity of Manuka honey persisted even after the removal of hydrogen peroxide by the enzyme [4]. An additional analysis in which prof. Henle research team diluted a water sample with Manuka honey (solution 15-30%) showed antibacterial behavior activity of Manuka honey (methylglyoxal concentration of 1.1 to 1.8 mm), while the commercial samples showed no reactive inhibition of the growth of bacteria in a dilution of water 80% [4].

Depending on the level of methylglyoxal, Manuka honey has different applications in medicine, for instance strengthening the immune system in gastrointestinal diseases (such as reflux or irritable bowel syndrome), it is used in the form of dressings in the treatment of bacterial infections of wounds and bedsores, its antimicrobial activity of in vitro in the treatment of wounds infected with *Staphylococcus aureus* and *Pseudomonas aeruginosa* [8].

Table 1. Distribution content of methylglyoxal in Manuka honey and their use

Product	The content of methylglyoxal (MGO)	The power of honey	Recommendations
MGO 100 +	100/mg/kg	Minimum	Strengthening the immunity and their well-being
MGO 250 +	250/mg/kg	Strong	Secondary health issues such as : indigestion, reflux
MGO 400 +	400/mg/kg	Very strong	The function of the natural antibiotic used for ulcers, irritable bowel syndrome, infected wounds
MGO 550 +	550/mg/kg	Super strong	Acute medical and treatment of chronic wounds

Source: Company information material Propharma.

Antioxidant properties of Manuka honey

Flavonoids, phenolic acids, aromatic acids and carotenoids are responsible for the antioxidant properties of honey [9]. It has been shown that the merger of simple sugars such as glucose and fructose also exhibit antioxidant activity [10]. It is the phenolic acids and flavonoids that exhibit health benefits for example: antiallergic agents, anticoagulants, anti-inflammatory and bactericidal. The contents of these active compounds in honey depends on the origin of the plant [11]. The study compared two Yao honey from Australia and New Zealand for the presence of the compounds like flavonoids, phenolic acid and abscisic acid using a HPLC method [6]. 15 flavonoids (average content of 2.22 mg / 100 g of honey) were isolated out of jelly Australian honey (*Leptospermum bush polygalifolium*), where the main flavonoids were identified as mircetyna and luteolin. In the case of honey from New Zealand Manuka (*Leptospermum scoparium* bush), the profile consisted mainly of flavonoids like quercetin and luteolin, the average content of total flavonoids was measured in the amount of 3.06 mg / 100 g body. The content of phenolic acids in the Australian honey was 5.14 mg / 100 g of honey, while in Manuka honey 14.0 mg / 100 g of honey. Almost three times the amount of the antioxidant was noted in the case of New Zealand honey in comparison with the honey obtained from the bush *Leptospermum polygalifolium* [6]. The last comparable component of the study was abscisic acid, which is derived from isoprene. Abscisic acid is not a fenolo - acid, but due to a similar chromatographic behavior, it is detected together with the fenolo - acid. It shows no biological activity in the human body, but is one of the most important indicators of the origin of honey [11]. In Australian honey, the abscisic acid content was twice as high as phenolic acids. The manuka honey abscisic acid level was 32.8 mg / 100 g of honey [6]. A study by Yao [6] showed that the flavonoid content in honey with phenolic acids may be helpful in identifying the floral honeys, and an additional confirmation of the origin of honey can be to determine the amount of abscisic acid. The results of the study cited above also allow you to find that Manuka honey has much greater antioxidant properties than other honey [6].

Manuka honey impact on pathogens in food

Recent years have been seen to promote the intake of minimally processed or completely natural food, as well as encourage humans to take advantage of the products widely available. One of the products under consideration in this application is honey, which is capable of inhibiting the growth of microorganisms in food [12]. As it has already been stated above, Manuka honey antimicrobial properties are dependent on the floral source of plant from which it is derived. The effect of inhibition of bacterial growth in food has been confirmed in numerous studies [13]. One of them put two food pathogens: *Listeria monocytogenes* and *Staphylococcus aureus* under the activity of honey from different parts of the world [14]. As far as *Listeria monocytogenes* is concerned, it is the only bacterium that passes through the barrier of placenta, and may cause the necrosis of the fetus. *Staphylococcus aureus*, in turn, can be present in a fermented type of food like sausages and cheese, where during the storage process, an uncontrolled formation of a dangerous substance called enterotoxin can occur [15]. In the study, Lee use six honeys from North America and two honeys produced in New Zealand. The test showed that honey from North America showed a lower antimicrobial activity in relation to food pathogens than the two Manuka honeys from New Zealand. Also, Manuka honey - MH1 was proved twice as likely to inhibit the growth of bacteria: *Bacillus subtilis* (51.5%) and *Bacillus cereus* (53.3%) compared to the total braking frequency obtained in the study. This product was not always the most effective, as exemplified by the bacterium *Salmonella enteritidis*, where the inhibition effect was the weakest of the entire group of the surveyed honey. In turn, the second Manuka honey in the study (designated as MH 2) had a 30% lower antibacterial activity against *Bacillus* [14].

Application of Manuka honey in medicine

The antibacterial properties of honey stem from a few factors, namely, its high concentration of sugars - mostly simple ones, low pH (4.0-4.5) and high osmotic pressure. Honey is easily absorbed by the human body, and, therefore, the presence of the minimum concentrations of vitamins, enzymes and minerals [16] contribute to the regeneration process [10].

Studies on the use of Manuka honey in medicine included the use of honey in improving the quality of life of patients with oncological diseases [17] and gastric ailments. Its effect on the growth of probiotic bacteria in the gut as well as the ability to prevent disease in the oral cavity [19] were also studied [20]. As a result of clinical experience, it was observed that patients treated for 10 days with skin cream containing Manuka honey (dosing the cream twice a day), indicated significantly reduced frequency of II grade dermatitis compared to people who used creams from drugstores [17].

Side effects associated with a head or neck radiation therapy in cancer patients include inflammatory conditions of the oral cavity. The application of aqueous lotion containing in its composition two drops of essential oil of *Leptospermum scoparium* bush caused a significant reduction in pain which appeared in the inflamed mucous membrane and, in result, a significant reduction of the inflammation [21].

Another department of medicine which uses health enhancing activity of manuka honey is gastroenterology. An example of Manuka honey use was to combat bacteria called *Helicobacter pylori* in the human stomach, which is proved to be an etiologic factor in case of ulcers. The study was performed using seven strains of bacteria isolated from gastric ulcers. The inhibition of growth of *Helicobacter pylori* was noted in the case of applying a 5% solution of Manuka honey. The total destruction of bacteria in the stomach was observed by the use of a concentration of 20% solution of Manuka honey. The experiment revealed strong inhibitory effect of this honey with respect to *H. pylori* [22].

The medical use of Manuka honey may also include the ability to stimulate the growth of intestinal probiotic bacteria. These properties were observed in Rosendale's study. It turned out that Manuka honey was an effective regulator of both maintaining and increasing the number of beneficial gut bacteria, which included *Lactobacillus rhamnosus* and *Bifidobacterium lactis*. This effect was particularly advantageous, because in proportion to the increasing number of probiotic bacterium, the number of pathogenic microorganisms in the intestine decreased.

Thanks to antimicrobial properties, Manuka honey has been applied not only in oncology and gastroenterology, but also in dentistry. Its presence helped to reduce the formation of plaque, reduce the symptoms of bleeding gums in the mouth [18], as well as inhibit the growth of *Streptococcus mutant* that causes dental caries [19].

Manuka honey and its role in healing of wounds

Honey can be used to treat various wounds such as pressure sores, infected cancer wounds, gangrenous and tuberculosis ulcers, diabetic sores, varicose veins, ulcers, necrosis of various origin, allergic skin disorders - lupus [2]. The advantages of the medical use of honey on wounds is the lack of side effects in the treatment of tissue, it is non-toxic, natural and easily available [23]. In vitro and in vivo showed honey's ability to retain moisture in the wound [1] so that the granulation of tissue in the infected wound occurs faster [24]. An additional advantage of honey, namely the natural presence of fructose, improves local nutrition of wounds and promotes rapid epithelialization process (the formation of a new layer of epidermis on the defects of the skin).

The barrier, which protects the wound and prevents the re-infection is the high viscosity of the honey [24]. Particularly noteworthy are the honeys having a high degree of viscosity, which largely depends on the floral source of honey [24]. A prominent among this range of honeys (Manuka honey) is derived from *Leptospermum scoparium* [25]. The antibacterial activity of Manuka honey also helps the pH by creating and maintaining optimal conditions for the operation of fibroblast, helping at the same time in the formation of collagen [24]. In vitro studies conducted on Manuka honey showed that treatment of wounds by applying honey may be partially related to the stimulation of wound inflammatory cells - cytokines into cells called monocytes, which are known to play an important role in healing wounds. The process of wound healing also includes the cleaning, which means a disinfection process, where using Manuka honey makes it possible to provide an alternative source of amino acids. They are present in the serum and dead cells of the wound, which are a culture medium for bacteria. Common complications of such bacterial infections are stenching wounds, especially in cases such as leg ulcers and diabetic foot [26]. As a result of implementing Manuka honey on the wound, the level of lactic acid increases, which acts antagonistically to the ammonia and sulfur compounds produced by the bacteria [24].

The clinical administration of Manuka honey reflected a particularly beneficial effect in the treatment

of wounds infected with a resistant strain MR96 808, where Manuka honey at a concentration of 1% caused a complete inhibition of such MRSA infected wound [27].

Tulle dressing containing Manuka honey maintains a moist environment and serves as a autolytic wound cleansing agent [28]. Dissolved honey layer prevents the dressing from sticking to the wound, allowing it to shift without tears of healthy tissue sections, which are very painful to a patient [24]. The absorption of secretions from the wound in Manuka dressings is 3.5 times higher than in dressings of other manufacturers. Hydrogel dressings with Manuka honey also accelerate the process of tissue regeneration in the treatment of wounds and difficult healing ulcers infected with *Staphylococcus aureus*. It was proved to take place because of the high concentration of methylglyoxal present in the honey.

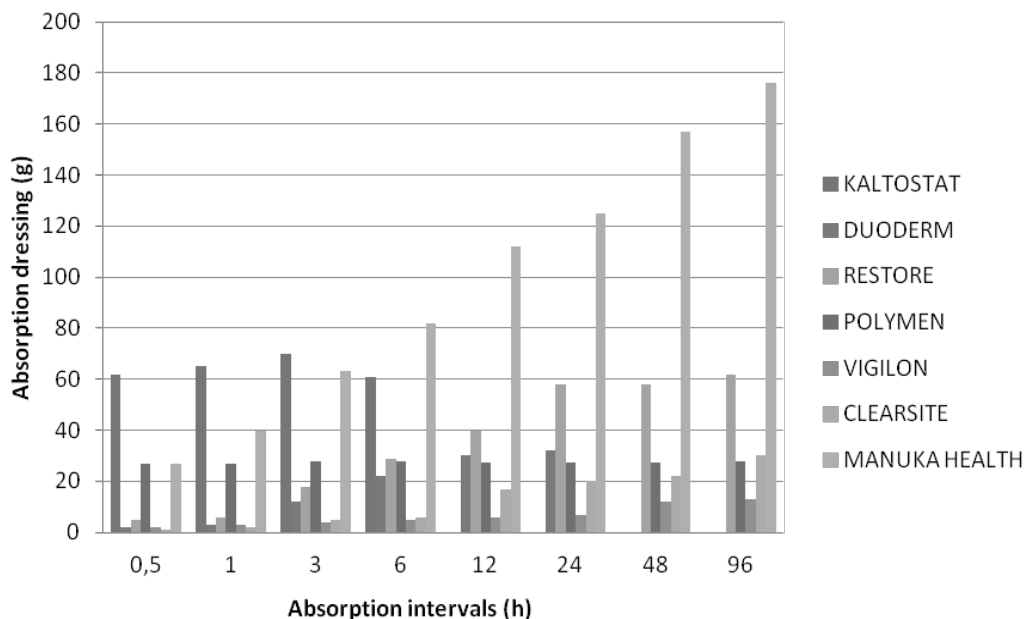


Figure 1. Comparison of absorption in Manuka dressing with other producers within specified time range
Source: Company information material Propharma.

Clinical studies show that Manuka honey has healing effects not only in infected wounds, but also acts as an anti-inflammatory agent [1] at a sensitive body location, like for instance the output of the catheter. Honey application results in reduced pain and swelling in the patient [24].

Prevalence and significance of kynurenic acid in Manuka honey

Kynurenic acid abbreviated to KYNA is a neuroactive metabolite of tryptophan. It is found mainly in the liver, kidney and brain, where it is synthesized in glial cells. The discovery of the acid was made in the second half of the nineteenth century by a German chemist Justus von Liebig, who detected the substance in the urine of dogs [29]. KYNA presence in food was reported in the largest amounts in bee products such as propolis, honey and bee pollen [30].

KYNA was examined to have neuroprotective and anticonvulsant effect. It was also shown that depending on the type of diseases of the central nervous system (schizophrenia, depression, epilepsy disease, Alzheimer's, Parkinson's, Huntington) kynurenic acid concentration in the human body is varied [29]. Taking into account the issue of athletes and special immunodeficiency stemming from stress and exercise, it may be worth to supplement the acid to prevent lowering the resistance of the nervous system.

The study of the KYNA acid content in honey was conducted by the Department of Toxicology of the Institute of Medicine in Lublin (in 2011).

KYNA content was examined by using the insulation of ion exchange resin Dowex 50W +. An analysis was performed using high performance liquid chromatography (HPLC) with fluorescence detection. The experiment revealed the presence of KYNA in all tested 69 samples. MGO 400 Manuka honey showed the highest KYNA content. It is worth noting that there was a significant difference in the content of MGO Manuka honey 400 compared to the other test batch of honey.

Table 2. Comparison of KYNA content in honey

Type of honey:	The average concentration of KYNA (µg/g of honey)
Manuk honey MGO 400	1.146
Manuk honey MGO 100	0.365
Linden honey producer: SąddeckiBartnik	0.402
Linden honey producer : Ratos – Natura	0.105
Buckwheat honey - producer : SąddeckiBartnik	0.374
Buckwheat honey - producer :Ratos – Natura	0.33
Buckwheat honey - producer :BartnikSokólski	0.262

Source: Company information material Propharma.

The average concentration of KYNA in linden honey was 0.252 ug / g of honey. In comparison, the average content in buckwheat honey was recorded in the amount of 0.322 ug / g of honey. The result obtained in buckwheat honey proves more pro-health value of this kind of Polish honeys.

The conducted study confirms the presence of KYNA in honeys. Despite the existing differences in the content of the acid between Manuka Honey MGO 400 and Polish honeys, it is important to stress out that the value of KYNA in linden honey produced by Sadecki Bartnik was higher than that obtained in Manuka MGO 100. This fact may contribute to the expansion of research on the effect of honey on the neurological system.

Conclusions

In Poland, honey is a particular food product that is valued for its health promoting properties known for centuries. The most widespread uses of honey in Poland include applying it in case of a common cold and a sore throat. Yet, it was shown that honey may also be used in medical dressings for wounds and pressure sores. In Poland, the use of native honey in such skin conditions is not very popular, but the emergence in the sale of New Zealand honeys for therapy treatment increased the interest in honey. As a result, Manuka honey is used in the treatment of wounds both in hospitals and at home.

This paper provided information on health benefits coming from the properties of Manuka honey. The high content of methylglyoxal in Manuka results in its widespread use in medicine. Manuka honey in a 20 percent solution was observed to reduce gastric complaints associated with the presence of *Helicobacter pylori* and after addition of two drops of oil, Manuka was observed to alleviate inflammation of the oral mucosa of patients undergoing radiotherapy. The high antimicrobial activity of Manuka honey has been observed against *Staphylococcus aureus*, which is one of the most sensitive of all pathogens.

Antioxidant and anti-inflammatory properties may be particularly beneficial in the diet and supplementation of athletes. A direct impact of honey on the health condition of this group has not been scientifically confirmed yet, but it may be an additional incentive for further research on healing and pro-health properties of Manuka. Background information on inflammatory lesions in an athlete's body, in particular in winter sports, where the person is constantly exposed to adverse external factors, states that some negative processes may be stopped by the supplementation of antioxidants as well as anti-inflammatory and deacidifying products. Therefore, it seems logical to encourage the supplementation with Manuka honey in athletes.

Moreover, Honey enhances the physical potential and endurance in athletes, both during trainings and during competitions. Its use after extensive exercise brings a fast relief, reduces symptoms of fatigue and ensures a rapid renewal of the expended energy. Studies have shown that honey intake between competitions or in the interval games allows for greater efficiency and a better tolerance of repeated effort [2].

Furthermore, acetylcholine present in honey, lowers blood pressure and improves blood circulation, choline has a protective effect on the liver and increases the secretion of bile. Metal ions stimulate the production of red blood cells and hemoglobin, which is an extremely important aspect in case of endurance athletes.

Many authors point to the advantages of honey over other food products administered to athletes. In a scale of products rapidly generating a large amount of energy, without causing digestive problems or other side reactions, honey received (a 1-10 scale) 9 points, glucose 7.5 point, and sugar beet (sucrose), only 4.5 points. The beneficial effects of honey are also confirmed in studies measuring the effectiveness of players. After honey intake, the efficiency rate was 48%, while after an administration of fructose, glucose or sucrose, it was noticeably lower (below 20%) [2].

Manuka honey may, therefore, have a particularly positive impact on the health of athletes, due to its non-specific chemical structure and unique health benefits. This finding requires confirmation in studies devoted

to Manuka honey supplementation in the group of athletes and their body's reaction to this substance. Present reports and experiments, however, give a very interesting outline on the impact of this product on homeostasis and prevention of health conditions.

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