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Review Article

# Differential Diagnostics of Chronic Diseases of Small Bronches in Children

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## Abstract

**Abstract:** The aim of the study is to create an automated decision support system for differential diagnostics of chronic nonspecific diseases of small bronchi in children.

**Materials and methods:** The questionnaire was taken as a basis, developed in the laboratory of pediatric pulmonology, Research Institute of Pulmonology, St. electronic versions. The information content of the signs of chronic diseases of the small bronchi was assessed. The threshold value of the responses was determined in points characteristic of a specific form of diseases of the small bronchi. To assess the quality of diagnostic decisions made by the system, generally accepted statistical indicators were used.

**Results and its discussion:** The test cards were filled in and the correctness of the assigned pathology probability scores was assessed in 113 children with BA, in 139 children with chronic bronchiolitis and in 103 children with bronchopulmonary dysplasia (BPD) and a history of BPD. A decision support system has been developed for the differential diagnosis of chronic nonspecific diseases of the small bronchi (CPMD) in children. The system assesses the likelihood of each pathology, which determines the conduct of informative and financially sound research methods for the final establishment of the pathology form. The main feature of this technique is the simplicity of obtaining results after 3-5 minutes from the beginning of filling out the test card. Approbation of the developed automated system for early detection in children at the outpatient stage made it possible to clarify the form of diseases of the small bronchi, conduct informative research methods to confirm the diagnosis, without using additional financial costs.

**Conclusions:** For the first time, an automated decision support system has been developed for the differential diagnosis of chronic nonspecific diseases of the small bronchi (CPMD) in children. The application of the developed system has confirmed its practical significance in the refinement of the form of CHNZMB in children. The true prevalence rates were many times higher than the published incidence data. Official statistics did not actually reflect the true state of the problem.

**Keyword:** Cannabis Sativa; Health; Hemp Seeds; Nutrition

## Introduction

Cannabis sativa L., commonly known as hemp, is a herbaceous plant belonging to the family Cannabaceae. Although its exact origin is not known due to its long history of cultivation, it is of Central Asian origin according to a common view (Farinon et al. [1]). Its cultivation is thought to have begun in China in 2800 BC. It spread from China to India and Iran and then to Europe. In the Middle Ages, hemp was grown extensively in Europe for use as a fiber, and its seeds were cooked with other grains (Apostol [2]). Hemp was an important crop in many European countries, including England, France, the Netherlands, Germany, Spain, and Italy during the Middle Ages and until the end of the sailing ship period (Carus and Sarmento [3]). In the past, it was traditionally produced as a fiber crop for textile and rope production. But since the first half of the 21st century, its cultivation has been reduced due to the increase in synthetic fibers and the use of some narcotic species of C. sativa L. (Farinon et al. [1]). Interest in hemp cultivation resumed in the

early 1990s when hemp cultivation was promoted in the European Union (Giupponi et al. [4]). While China is the largest hemp-producing and exporting country, more than 30 countries grow hemp. Europe and Canada are also at the forefront of the global hemp market. The global hemp market is estimated to consist of more than 25,000 products. Currently, industrial hemp has many uses. For example, the construction and insulation industry, paper and textile industries, and food and nutrition are the main markets, while the cosmetics and automotive industries are growing (Crini et al. [5]).

Cannabis is grown mainly for three main purposes: industrial, narcotic/recreational and medicinal (Farinon et al. [1]). For forensic and legal purposes, the most important classification of cannabis species is the fiber type (hemp) and drug type (marijuana or indica) (Giupponi et al. [4]). Two cannabis cultivars grown worldwide are Cannabis sativa L. and Cannabis sativa indica. The biggest difference between the two plant species is their appearance and the amount of delta-9-tetrahydrocannabinol (THC), a psychoactive cannabinoid. Generally, industrial hemp (Cannabis sativa L) contains low levels of THC of less than 0.3%, while varieties of Cannabis indica grown for use as medicine may contain between 2% and over 20% THC. Today, 26 hemp varieties containing low levels of THC have been certified for cultivation in the European Union (Apostol [2]). In most European countries, the current upper legal limit for the cultivation of hemp for fiber and seed production is 0.2% THC on a dry basis (Frassinetti et al. [6]).

## Cannabidiol

Unlike THC, another important cannabinoid that is psychotropically inactive is unregulated cannabidiol (CBD). CBD levels tend to be higher in C. sativa grown for seeds or fibers (Giupponi et al. [4]). Non-psychoactive CBD is an interesting pharmaceutical and food supplement derived from industrial hemp. Recently, CBD has gained increasing importance in the pharmaceutical and dietary supplement industries. CBD can be easily extracted as a high-value by-product from the flowers and leaves of industrial hemp (Carus and Sarmento [3]). Cannabis varieties called "industrial hemp" often contain a high concentration of cannabidiol acidic precursor (CBDA). This compound is known to have a wide variety of important biological properties, including anticonvulsive, anti-epileptic and antimicrobial activities. It is also used as a supplement in the treatment of osteoarthritis and musculoskeletal diseases (Izzo et al. [7]).

## Hemp seeds

Cannabis sativa L. is a non-drug type of cannabis, and its seeds (hemp seeds) are an important source of dietary oil, fiber, minerals and protein (Apostol [2]). The hemp seed is the part of the fruit that looks like a small walnut approximately 3-6 weeks after the female flower is fertilized (Crescente et al. [8]). Although hemp leaves, sprouts and flowers can be consumed as raw food by preparing juices and salads, hemp seeds are the most common part of the cannabis plant consumed as food (Cerino et al. [9]). In the past, hemp seeds were (traditionally) generally considered a waste product and used as animal feed. However, recently, with the understanding of the nutritional properties and health benefits of hemp seeds, its production has increased, and it has become a product with a potential market (Farinon et al. [1]). Indeed, it has been used in traditional oriental medicine for thousands of years to treat various disorders (pain, wounds and skin diseases, cough, blood problems, constipation, jaundice, and colic) (Crescente et al. [8]).

All hemp food products originate from hemp seeds or products such as meal, flour (ground seed after oil extraction), protein powder, oil and bioactive substances from these seeds. All these products are gaining increasing popularity in human nutrition as an important food source (Crini et al. [5]). Hemp seeds have a high nutritional value and are rich in phytosterols, ω-3 and ω-6 essential fatty acids, and proteins (about 25% dry weight) containing all essential amino acids. For these reasons, hemp seeds have started to be used in various food products with high nutritional properties. Various products with added varying amounts of hemp flour, including high fiber pasta (10-20% hemp flour), as well as reduced-fat cakes and biscuits are already on the market (Mamone et al. [10]). In addition, hemp milk, which is made from a combination of hemp seeds and water, is an alternative plant-based milk that is increasing in popularity and for those who are allergic or intolerant to cow's milk (Curl et al. 2020). Roasted seeds are popular snacks in China. Also, hemp seed oil has long been used in Russia and many other Eastern countries. It has been added as a food additive to bread, yogurt, cookies or meat cutlets (Lukin and Bitiutskikh[11]; Zając et al.[12]). It has been shown that with hemp flour added to the bread at a rate of 10%, high nutritional value bread containing 27.4% more proteins, 200.8% more fats and 497.2% more fibers is produced (Lukin and Bitiutskikh [11]).

## Nutritional properties of hemp seeds

Hemp seeds provide ~500–600 kcal/100 g of energy and consist of approximately one-fourth of protein, one-fourth of carbohydrate and one-third of fat, with some important differences between different genotypes (Cerino et al. [9]). Hemp seeds contain vitamins and minerals of biological importance. In addition, hemp seeds have significant potential for fiber (Apostol [2]). Whole hemp seeds contain approximately 25-35% balanced fat content, 20-25% easily digestible protein rich in essential amino acids, 20-30% carbohydrates, mostly consisting of dietary fiber (10-15%), and additional vitamins and minerals (Leizer et al. [13]). Hemp fiber mostly (80%) consists of insoluble fractions (Callaway [7]). After removing the hull, the edible part of the seeds contains on average 46.7% oil and 35.9% protein. The carbohydrate fraction is greatly reduced (to about 10%). The concentration of antinutritional compounds such as phytic acid, concentrated tannins and trypsin inhibitors is very low in hemp seeds (Brenneisen [14]; Wang and Xiong [15]). Hemp seeds have rich protein content which is consists of about one-third of albumin, an important protein also found in egg whites and human blood, and two-thirds of edestin, another

important globular protein of similar character. Unlike soybeans, which contain the inhibitory factor trypsin, hemp seeds are easily digestible by human body (Apostol [2]).

Hemp seeds are rich in mineral arrays such as phosphorus, potassium, sodium, magnesium, sulfur, calcium, iron and zinc, and vitamin E (Frassinetti et al. [6]). Hemp seeds contain high amounts of phosphorus (1160 mg/100g), potassium (859 mg/100g) and magnesium (483 mg/100g) (Rodriguez Leyva and Pierce [16]). It has been reported that consumption of low amounts (about 50 mg) of hemp seeds can provide 50-100% of various minerals including copper, magnesium and zinc and >100% of vitamins A, D and E (Andrews et al. [17]). In addition to its nutritional value, hemp seeds are also rich in natural antioxidants and other bioactive components such as bioactive peptides, phenolic compounds, tocopherols, carotenoids and phytosterols, the content of which is mostly influenced by factors such as environmental, agricultural and partially genetic variability (Farinon et al. [1]).

## Hemp seed oil

The nutritious hemp seeds can be consumed raw or made into hemp seed oil, which has an excellent and unique fatty acid profile (Carus and Sarmento [3]). Hemp (Cannabis sativa L.) seed oil is valued primarily for its nutritional properties and associated with health benefits (Leizer et al. [13]). The main value of hemp seeds and oil comes from the fatty acid composition of the ω-3 and ω-6 classes, which are essential for many physiological processes, including the maintenance of cell membrane structure, synthesis of prostaglandins and leukotrienes (Crescente et al. [8]). Hemp seed composition and oil yield are affected and vary by many factors such as seed variety and climate. Overall, 33 different fatty acids, particularly polyunsaturated fatty acids such as linoleic acid (50-60%) and α-linolenic acid (20-25%) have been identified in hemp seed oil (Abdollahi et al. [1]). Previous studies have shown that hemp seed oil is characterized by high polyunsaturated fatty acids (PUFA) content and low saturated fatty acids (SFA) content. More precisely, based on genotype and environmental factors, hemp seed oil contains up to 90% unsaturated fatty acids, 70% to 80% of which are PUFAs (Farinon et al. [1]). Saturated fatty acids (especially palmitic and stearic) appear only around 10% in hemp seed oil (Crescente et al. [8]). In their study on seven different varieties of hemp seeds ("Bialobrzeskie", "Felina 32", "Tygra 75", "Futura 27", "Santhica", "Fedora 17" and "Finola"), Irakli et al. [18] showed that the "Finola" variety had the highest content of γ-linolenic and α-linolenic acids and the lowest content of oleic acid and saturated fatty acids such as palmitic and stearic acids.

Hemp seed oil contains linoleic acid (18:2, n-6, LA) and α-linolenic acid (18:3, n-3, ALA) as the major omega-6 and omega-3 polyunsaturated fatty acids, respectively. These fatty acids constitute the most desirable content of the oil, especially because of the proportions in which they are present. It has been reported that the ratio of linoleic acid and α-linolenic acid (LA:ALA) in the composition of the hemp seed oil is between 2:1 and 3:1 (Leizer et al. [13]; Crini et al. [5]). Izzo et al. [7] showed a good ω-6/ω-3 ratio in the thirteen different hemp seed oils they studied, ranging from 1.71 to 2.27. The presence of caryophyllene (740 mg/L), myrcene (160 mg/L), sitosterol (100-148 g/L) and traces of methyl salicylate in the oil have also been reported. Trace amounts of CBD have also been detected (Leizer et al. [13]). The proper ratio of fatty acids and higher intake of ω-3 fatty acids can provide appropriate amounts of prostanoids and leukotrienes with anti-thrombotic, anti-vasoconstrictive and anti-inflammatory properties. Thus, it can reduce the risk of other chronic diseases such as Alzheimer's disease, inflammatory bowel disease, obesity, rheumatoid arthritis, as well as coronary artery disease and other cardiovascular problems (Patterson et al. [19]). It is known that PUFA increases the oxidation rate of unsaturated fatty acids and also decreases hepatic lipogenic enzymes (malic enzyme), fatty acid synthase and glucose-6-phosphate dehydrogenase, resulting in lower plasma and tissue triglyceride concentrations (Vispute et al. [20]).

In addition to LA and ALA from n-6 and n-3 fatty acids, hemp seed oil contains the biological metabolites γ-Linolenic Acid (18:3, n-6, GLA) and Stearidonic Acid (18:4, n-3, SDA), which facilitate the conversion of long-chain PUFAs to their biologically active form (Farinon et al. [1]). In addition, GLA also performs an anti-inflammatory activity as it is rapidly converted to Dihomo-γ-Linolenic Acid (DGLA; 20:3, n-6) in the human body. In addition, GLA can be converted to PGs series-1, another group of eicosanoids with potential anti-inflammatory and immunomodulatory effects. DGLA resides in the cell membrane, can act as a precursor of anti-inflammatory metabolites and compete with Arachidonic Acid (20:4, n-6, AA) for the synthesis of metabolites involved in the inflammatory response (Sergeant et al. [21]; Veselinovic et al. [22]). The additional presence of GLA in hemp seed oil ultimately makes its nutritional value superior to most comparable seed oils (Leizer et al. [13]). These results further strengthen previous reports that the relative proportions and composition of hemp oil fatty acids are ideal for human nutrition. In folk medicine, hemp seeds have a positive health effect in lowering cholesterol and blood pressure. In addition, hemp seed oil may contribute to the prevention of cardiovascular diseases (Babiker et al. [23]).

## Hemp seed protein

Hemp seeds have a rich protein content, and the main proteins are globulin/edestin (60–80% of the total protein content) and albumin, which are easily digestible in the gastrointestinal tract. However, there is insufficient information on the structural and functional properties of seed globulin and albumin fractions. Hemp seeds also contain all nutritionally important amino acids, especially high levels of arginine and glutamine amino acids (Wang and Xiong [15]; Crini et al. [5]). Arginine accounts for approximately 12% of hemp seed protein compared to less than 7% for most other food proteins, including proteins from potatoes, wheat, corn, rice, soy, rapeseed, egg whites and whey. Arginine acts as a very important signal messenger in the cardiovascular system. Arginine, which has beneficial cardiovascular properties, is a precursor of the vasodilating agent nitric oxide, which increases

blood flow and contributes to the maintenance of normal blood pressure (Rodriguez Leyva and Pierce [16] ; Aluko [24], Crescente et al. [8]; Wang and Xiong [15]). The Arg/Lys ratio is a determinant of the cholesterolemic and antherogenic effects of a protein. The Arg/Lys ratio of hemp protein (3.0-5.5) is significantly higher than that of soy protein isolate (1.41) or casein (0.46), making hemp protein especially valuable as a nutritious and bioactive ingredient for the formulation of foods that support cardiovascular health. In addition, hemp seed proteins represent a source of the sulfur-containing amino acids cysteine and methionine. The total sulfur-containing amino acids range from 3.5% to 5.9% (Aluko [24]; Wang and Xiong [15]). It has been stated that unlike soybeans, hemp seeds contain very low amounts of anti-nutritional factors such as trypsin inhibitors and therefore are more digestible (Mamone et al. [10]). The high digestible protein content and the absence of trypsin inhibitors found in soybeans increase the nutritional value of these seeds (Vispute et al. [20]). In particular, hemp meal obtained after oil extraction from hemp seeds contains abundant high-quality storage proteins. The protein content of hemp meal varies from 30 to 50 percent in dry matter, depending on the hemp variety and oil extraction method (cold pressing or solvent) and yield (Wang and Xiong [15]). Hemp seed protein is of great interest in both scientific and industrial fields because of its excellent nutritional value and superior digestibility. On the other hand, a wide range of products such as beverages, functional ingredients, nutritional supplements, and various personal care products have been developed from hemp proteins in the food industry (Wang and Xiong [15]).

## Hemp seeds and health

The results obtained from a study investigating the nutraceutical effect of hemp seeds showed that C. sativa seeds are rich in beneficial bioactive compounds and have antioxidant activity in vitro and ex vivo, as well as antimutagenic activity (Frassinetti et al. [6]). In addition, the high amount of linoleic and linolenic fatty acids, which are essential fatty acids, in hemp seeds is valuable for health. Amino acids found in hemp seeds are also known to improve the functions of the liver, pancreas and nervous system (Wolfe [25]). In vitro and in vivo studies in rats have shown that peptides isolated from hemp seeds have the potential to be used as antioxidant and antihypertensive agents (Apostol [2]).

## Antioxidant activity

An imbalance between the production of reactive oxygen species (ROS) and the availability of adequate endogenous antioxidants can lead to the progression of chronic diseases, inflammation and carcinogenesis by causing oxidative stress at the cellular level, with damaging effects on membranes, proteins, enzymes and DNA (Frassinetti et al. [6]). However, the high PUFA content in hemp seed oil makes it highly susceptible to lipid oxidation. Oxidative instability is one of the most important factors responsible for reducing oil quality and shelf life (Izzo et al. [7]). However, edible hemp sources are rich in antioxidant components, including a wide variety of terpenes, phenols, especially stilbenoids and lignanamides (Moccia et al. [26]) and phenolic compounds prevent product degradation by inhibiting radical reactions responsible for lipid oxidation (Babiker et al. [23]). A wide variety of polyphenols, especially flavonoids such as flavanones, flavanols, flavonols and isoflavones, have been identified in hemp (Irakli et al. [18]). The hemp seed oil contains other minor components such as polyphenols, carotenoids and tocopherols, all of which are involved in antioxidant processes, which may play an important role in protecting edible oils against lipid oxidation. In humans, all these compounds may exhibit important biological properties such as antioxidant and anti-inflammatory effects (Izzo et al. [7]). Chlorophyll (0.041–2.64 μg/g), carotenoid (0.29–1.73 μg/g), total phenols (22.1–160.8 mg Gallic Acid Equivalent (GAE)/g), and tocopherol (3.47-13.25 mg/100 g) contents of thirteen different hemps studied by Izzo et al. [7] to determine the bioactive component content in hemp seed oil varied greatly.

## Anti-inflammatory effect

The hemp seed oil contains 80% PUFAs, high concentrations of phytosterols (eg sitosterol and campesterol), α, γ-linoleic acids, as well as essential fatty acids. Because of these properties, it can be identified as useful phytotherapeutic against a wide variety of lipid-related diseases (Callaway [27]; Kaushal et al. [28]). In addition, lignanamides in hemp seeds are powerful antioxidant and anti-inflammatory agents (Luo et al. [29]). Apart from amino acids and fatty acids, hemp seeds are rich in lignanamides such as cannabisin A, B, C, etc., caffeoyltyramine-like compounds, and other polyphenols. Phenylpropionamide (TPA) is the common component of these ingredients (Zhou et al. [30]). The TPA composition of cannabis seeds and their effects on neuroinflammation biomarkers and memory impairment were investigated by Zhou et al. [30]. In the study, fourteen TPAs were identified in the cannabis seed extract. The anti-neuroinflammatory effect of the TPA extract was evaluated using a lipopolysaccharide (LPS)-induced mouse model. TPA prevented LPS-induced learning and spatial memory damage. Moreover, increased IL-1β, IL-6 and TNF-α brain levels in LPS-induced mice were reduced by TPA treatment. In addition, TPA attenuated LPS-induced hippocampal neuronal damage in mice. Potential anti-inflammatory and antioxidant properties of hemp seeds were investigated in high-fat diet-induced fatty liver disease model rats, thanks to beneficial phytochemical properties such as optimal omega-6: omega-3 PUFA ratio. The results revealed that hepatoprotective effects were observed in rats given hemp seed lipid fraction, and this effect was mediated by the inhibition of oxidative stress and inflammatory mediators such as Cox-2, hPGDS, mPGES, IL-4, TNF-α and sEH. In conclusion, the study suggests a plausible antioxidant and anti-inflammatory role of hemp seed lipid fractions in alleviating pathophysiological conditions, including fatty liver disease, where oxidative stress and inflammation are key mediators (Kaushal et al. [28]).

## Cardiovascular health

Hemp oil has been widely recognized to have a number of health benefits, such as cholesterol-lowering properties and lowering high blood pressure, due to the presence of two essential fatty acids (linoleic acid and α-linolenic acid). The ratio of n-6 to n-3 PUFAs in hemp seeds is optimal (3:1), which is important for

cardiovascular health (Kaul et al. [31]). This is because PUFAs, especially those from the n-3 family, can improve lipid metabolism due to their ability to induce fatty acid oxidation in liver and skeletal muscle and simultaneous suppression of hepatic lipid synthesis (Clarke [32]; Jurgoński et al. [33]). In addition, n-3 PUFAs can reduce inflammation in the body and lipid deposition in blood vessel walls and lower blood pressure (Lunn and Theobald [34]). At the same time, hemp seeds are also rich in peptides considered as a potential antihypertensive agent and lignan amides with potential anti-inflammatory and cardiovascular activities (Flores-Sanchez and Verpoorte [35]; Girgih et al. [36]; Majewski and Jurgoński [37]). However, it has also been shown that the cardiovascular positive effects of hemp seeds are not only due to the fatty acids it contains. Relatively potent hypolipidemic effects of dietary hemp were observed in genetically obese rats, with the fat fraction only partially responsible for these effects (Opyd et al. [33]). Majewski and Jurgoński [37] supplemented 8-week-old obese male Zucker rats with ground hemp seeds (12% diet) or lipid fractions in the form of hemp seed oil (4% diet) for 4 weeks. Hemp seed oil reduces blood plasma HDL-cholesterol (x0.76, $p \leq 0.0001$), triglycerides (x0.55, $p = 0.01$), while hemp seeds reduce HDL-cholesterol (x0.71, $p \leq 0.0001$) and total cholesterol (x0.81, $p = 0.006$). Hemp seeds and oil reduced lipid peroxidation (malondialdehyde) in blood plasma and heart, and improved noradrenaline contraction. However, acetylcholine-induced vasodilation was only enhanced by hemp seeds. Ultimately, dietary supplementation with ground hemp seeds was found to be much more beneficial than hemp seed oil, suggesting that lipid fractions were only partially responsible for this effect.

Jurgonski et al. [33] compared the effects of natural or partially defatted hemp seeds on intestinal function, antioxidant status, and lipid metabolism in rats fed a high-fat (HF) diet. Feeding with an HF diet caused obesity and several metabolic disorders in rats. Supplementation of the HF diet with both seed forms increased cecal short-chain fatty acid concentrations and improved the antioxidant status of rats, particularly glutathione metabolism in the liver. Dietary consumption of defatted seeds decreased liver triglyceride accumulation while negatively increasing liver cholesterol content. In contrast, dietary consumption of natural seeds decreased plasma cholesterol concentration, particularly the non-HDL fraction, and increased PPARγ hepatic expression. The study showed that dietary supplementation with relatively small amounts of natural or defatted hemp seeds can partially alleviate the disorders it causes, although it cannot prevent the development of obesity in rats fed a high-fat diet.

Recently, natural products have attracted attention as alternative strategies to treat hypercholesterolemia and related pathologies. Statins have classically been used as first-line therapy to inhibit cholesterol synthesis and mediate the clearance of LDL-C receptors from the blood, thereby lowering LDL levels. However, chronic use of statins plays a role in hepatic damage, myalgia, clinical rhabdomyolysis, neural problems, and kidney pathologies (Thompson et al. [38]). Kaur et al. (2021) demonstrated the curative and therapeutic potential of hemp seed lipid fractions against hypercholesterolemia-related nephropathies and other systemic effects. In the study, hemp seed lipid fractions were prepared. Their curative effects on HF-induced lipid profiles, kidney function markers, histopathological/morphological changes, renal oxidative stress and inflammation markers were examined and compared with those of statins. The administration of hemp seed lipid fractions not only improved the lipid profiles and morphological signs of hypercholesterolemia but was also found to be safer in terms of liver and kidney function markers compared to statins.

## Anti-carcinogenic effect

Moccia et al. [26] investigated the capacity of polar extracts of edible sources (seed, flour and oil) from the Fedora cannabis variety to inhibit cell growth and induce apoptotic cell death in two different cell lines, Caco-2 and HT-29, derived from human colorectal adenocarcinoma. Extracts from hemp seed and flour did not interfere with Caco-2 and HT-29 cell growth, while the extract from oil (150 μg/mL) significantly reduced cell viability after 24 hours of treatment. This effect is associated with the activation of apoptotic cell death and is independent of the antioxidant capacity of the polar oil extract.

## Hypoallergenic feature

Hemp-based food products are considered less allergenic than other edible seeds. Mamone et al. [10] examined in vitro hemp protein isolate (HPI) derived from hemp flour, a residue of hemp seed oil extraction, to test the hypoallergenic property of hemp seed. All known cannabis allergens, including thaumatin-like protein and lipid transfer protein (LTP), were completely eliminated by the HPI production process, and no part of the proteins could be detected after gastrointestinal digestion. These data support the use of HPI as an ingredient in hypoallergenic foods [39-41].

## Effect on the nutritional value of animal foods

There are studies on the use of hemp seeds in livestock and the effect on the nutritional value of animal foods. Various effects are suggested in relation to the nutraceutical properties of cannabis derivatives added to basal feeds, such as a reduction in the rate of tibia deformation (in poultry), a better serum lipid profile, protective effect on the development of liver diseases, antimicrobial activity, promotion of antioxidative systemic state, and anti-inflammatory activity. Another important aspect of the integration of hemp seed products into animal feed is the enrichment of ω-3 PUFA content and its positive effect on the fatty acid composition of meat, eggs and milk (Della Rocca and Di Salvo 2020). Dietary supplementation of 0.3% hemp seed added to broiler chicken feed by Vispute et al. [20] did not affect growth performance and carcass characteristics; however, it positively altered the serum lipid profile of poultry and improved gut health. The total number of coliform bacteria in the jejunum of the birds decreased, and the total number of lactobacillus bacteria in the cecum of the birds increased significantly. While the serum protein concentration remained unchanged, significant reductions in serum lipids such as triglyceride, LDL and total cholesterol concentration were noticed.

AST serum enzyme concentrations were significantly reduced. It is thought that thymoquinone, sterols, flavonoids, alkaloids, soluble fiber and PUFA in cannabis seeds may have contributed to the synergistic reduction of total and LDL cholesterol content (Vispute et al. [20]).

Vodolazska and Lauridsen (2020) compared the effects of dietary hemp seed oil with soybean oil on the nutritional status of lactating sows and piglets. The highest proportions of C18:3n-3, C18:4n-3 and C20:4n-6 were obtained from the mature milk of sows fed a 5% hemp seed oil diet compared to other dietary oil sources (5% soybean oil or a 50:50 mix of hemp and soybean oil at 5%). The addition of 5% hemp seed oil to lactating sow diets reduced the ratio of n-6/n-3 in the milk of sows and plasma of both sows and piglets compared to diets containing soybean oil. In addition, the number of stillbirths decreased in sows fed the hemp seed oil diet from day 103 of pregnancy compared to those fed the other diets [42-44].

## Conclusion

Cannabis sativa L., commonly known as hemp, provides numerous health and economic benefits with commercial applications such as seed production, fiber, oil and pharmaceutical applications. Hemp seeds, which are rich in nutrients and supported by an increasing number of studies in recent years, are becoming an important alternative source in the food and nutraceutical industry. The demand for hemp seeds is expected to increase rapidly as consumers worldwide are increasingly interested in ingredients derived from natural sources. With the right quality management and marketing, the use of hemp seeds and oil in healthy human nutrition will constantly expand.

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