Letters In Health and Biological Sciences

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Mini Review Open Access

A Mini Review on Medicinal Effects of Edible Bird's Nest

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Abstract

Edible bird's nest is a famous and nutritious food which is well-known among Chinese community. It is made from the saliva of swiftlets. It is consumed for various reasons, including as health tonic, complexion enhancer, asthma alleviator and immune system enhancer. It contains both macronutrients and micronutirents such as carbohydrates, glycoproteins, calcium, sodium, magnesium, zinc, manganese, iron and others. To date, a number of studies have reported on the health benefits of EBN consumption. Hence, this review describes the various medicinal values of EBN.

Received Date: April 28, 2017
Accepted Date: June 4, 2017
Published Date: June 6, 2017

Citation: Chye, S.M., et al. A Mini Review on Medicinal Effects of Edible Bird's Nest. (2017) Lett Health Biol Sci 2(1): 65-67

DOI: 10.15436/2475-6245.17.016

Introduction

Edible bird's nest (EBN), also known as the "Caviar of the East", is a renowned delicacy among Chinese community for its nutritional and medicinal value[1]. EBN is made from the saliva of tiny cave-dwelling birds known as swiftlets that are commonly found in Southeast Asia, including Malaysia[2]. The first consumption of EBN dated back into the Tang Dynasty (618 - 907 A.D) where it was served to the courts of the China's Emperor as a supreme delicacy. Since then, the medicinal benefits of EBN have been carefully documented and it was later recognized as one of the great four tonics in Traditional Chinese Medicine during the late Ming (1405 - 1433 AD) and early Ching (1644 - 1911 AD) Dynasties[1,3]. Due to its scarcity and rarity, EBN was regarded as a symbol of wealth, power and prestige[3]. For centuries, EBN had been consumed as health tonic, complexion enhancer, asthma alleviator and immune system enhancer[2].

The major nutrient components of EBN are carbohydrates and glycoproteins, along with minor essential trace elements such as calcium, sodium, magnesium, zinc, manganese and iron[2,3]. EBN contains many bioactive compounds which have health promoting effects such as glucosamine, lactoferrin, sialic acid, amino acids, fatty acids, triacylglycerol, vitamins, minerals and other antioxidants[3-5]. Despite many health effects were claimed to be associated with EBN consumption, its mechanism of action is unknown and there is no clinical evidence to support those claims. This article aims to provide an overview on EBN and its medicinal effects, with support from the latest evidence-based discoveries on the benefits of EBN consumption.

Medicinal Effects of EBN

Antiviral properties of EBN

In 2006, a research was conducted to study the antiviral efficacy of natural cave and house-cultured EBN[4]. The research demonstrated that EBN extract could effectively inhibit influenza infection independent of its strains− human, avian and swine, by directly binding to the influenza virus itself or inhibiting the hemagglutination of the virus to human erythrocytes (Figure 1). Furthermore, EBN was found to neutralize the virus infection in Madin-Darby canine kidney (MDCK) cells. In the experiment, EBN extracts treated with the protease pancreatin, has shown a stronger inhibitory activity against influenza virus, indicating that the lower molecular peptides (10 - 25kDa sialyl glycoprotein) were accounted for the antiviral properties of EBN. Conversely, EBN extracts treated with neuraminidase (NA), which cleaves the terminal sialic acid residues, causes reduction in the EBN/virus binding activity. This suggests that the virus binding effect of EBN is related to the presence of sialic acid. Generally, the viral inhibition activities of the wild EBN extracts were higher than the house-cultured EBN extracts. It was proved that the main antiviral effect of EBN was mediated by the sialyl glycol conjugates with Neu5Ac2-3Gal linkages. The study concluded that EBN could be a safe and effective natural source for the

prevention of influenza virus infection. However, the detailed *in vivo* effects of the influenza virus inhibition by EBN should be evaluated. Later in 2008, Yagi et al., reported the presence of N-glycosylation in EBN and proposed that the sialylated high antennary N-glycans of EBN, particularly, tri-antennary N-glycan bearing the a 2,3-N-acetylneuraminic acid residues, contributed to the inhibition of viral infection[5].

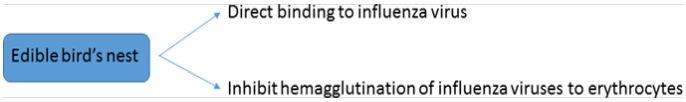

Figure 1: Anti-influenza virus effects of edible bird's nest.

The antiviral activity of EBN is further supported in the 2016 study by Haghani and his colleagues[6]. The bioactive sialic acids or thymol derivatives in EBNs have shown to effectively inhibit the virus IAV strain A/Puerto Rico/8/1934 (H1N1) by decreasing the viral intracellular NA and extracellular non-structural protein 1 (NS1) genes which are required for the viral infection initiation and replication, respectively. However, these effects were only observed in untreated EBN. EBN which received enzymatic treatment (either pancreatin or NA) showed no effect on the NA gene, while EBN with pancreatin treatment showed increased extracellular NS1 copy number and reduced immunomodulatory property[6]. The observations suggested that some amino acids of EBN might cause an increase in the viral activities. On the other hand, EBN has shown to improve the outcome of influenza infection in BALB/c mice through modulation of immune responses by actively changing the cytokines patterns, such as activation of pro-inflammatory responses and cell-mediated immunity, depending on the infection phases. On top of that, pre-treatment with EBN showed protective effect against the virus in the mice. EBN which contains higher amount of acetylated sialic acid (Neu 2,4,7,8,9Ac6) displayed better antiviral activity regardless of the source locations they were obtained. It is recommended, however, to examine the bioactive metabolites of EBN before using it as an alternative antiviral medicine in clinical trials as the origin of EBN and the species of swiftlets might affect the EBN's composition.

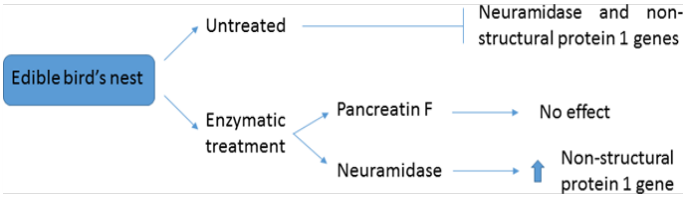

Figure 2: Anti-H1N1 virus effects of edible bird's nest.

Anti-oxidant properties of EBN

Apart from antiviral activities, EBN is also well-known for its antioxidant properties. An *in vivo* study was carried out to elucidate the antioxidant and anti-inflammatory effects of EBN on high fat diet (HFD)-induced oxidative stress and inflammation in rat models[7]. The results demonstrated that EBN attenuated the HFD-induced oxidative stress and inflammation via transcriptional regulation of hepatic antioxidant and inflammation-related genes; and the effects were better than Simvastatin, a well-known lipid-lowering medication. In short, the study supported the use of EBN as an effective supplement for the prevention of obesity-related inflammation and oxidative stress.

The ability of EBN in reducing oxidative stress is believed to be attributed by its antioxidant content, as demonstrated in a study conducted by Yida et al.[8]. The EBN samples were first subjected to a simulated gut digestion model, and the digested samples were then tested for their antioxidant activities. Results showed that the digested samples displayed potent antioxidant activities that contributed to the reduction in oxidative stress markers. Similarly in another study, EBN displayed protective effect against hydrogen peroxide-induced toxicity in SH-SY5Y cells[9]. Hydrogen peroxide is a chemical which induces oxidative stress in cells. The protective effect of EBN suggested that it had the ability to scavenge free radicals and decrease radical oxygen species, thereby lowering the oxidative stress. Hou et al., further suggested that the antioxidant properties of EBN were conferred by its constituents, namely lactoferrin and ovotransferrin[9].

Neuroprotective effects of EBN

Several studies investigated that the neuroprotective effects of EBN were reported. Hou et al., demonstrated that EBN attenuated cortical and hippocampal neurodegeneration in ovariectomized rats[10]. The data obtained showed that EBN supplementation improved estrogen deficiency-induced neurodysfunction by reducing advanced glycation end-products in serum and down-regulating genes associated with neuro-degeneration and apoptosis in the hippocampus and frontal cortex. Similar findings were observed in another study whereby EBN conferred the neuroprotective effects against 6-hydroxydopamine-induced degeneration of dopaminergic neurons principally through inhibition of apoptosis. Thus, it could be concluded that EBN might serve as a novel alternative therapy for oxidative-stress mediated neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease[11].

Effects of EBN on cardiometabolic diseases

To date, several studies which employed HFD or ovariectomized rat models have reported that EBN might possess beneficial effects on cardiometabolic diseases such as diabetes and cardiovascular diseases (CVD)[12-14]. HFD and the lack of hormones in ovariectomized rats worsen the metabolic indices (such as increased leptin and decreased adiponectin) and lipid profile. This would induce hypercholesterolemia along with insulin resistance, a condition which contributes to an increased risk for developing cardiometabolic diseases. Adiponectin and lectin are both important regulators of lipid metabolism and coagulation, whereby high metabolic indices are reflected by high adiponectin level and decreased level of leptin. In these studies, EBN has been proven to improve lipid profile and metabolic indices in rats, in comparison to the non-treated and Simvastatin-treated groups[12-14]. The effects were possibly mediated through the regulation of coagulation-related genes and insulin signalling genes.

Effects of EBN on bone regeneration

The effects of EBN on bones and cartilages were also investigated in several studies. Matsukawa et al., showed that ovariectomized rats fed with EBN had improved femur bone strength accompanied with an increase in dermal thickness[15]. It was also observed that oral administration of EBN significantly produced rats with heavier body weight along with higher fe-

mur calcium, phosphorus and hydroxyproline concentration as compared to the control group. Generally, the ovariectomized rats provided with high EBN supplementation showed greater improvement as compared to the rats given low EBN supplementation. However, the administration of EBN did not affect the serum estradiol concentration. Skin samples collected from the rats were stained with Masson's trichrome staining to evaluate the thickness of collagen fibrils. Results from the histological evaluation show that EBN treatment was able to increase the dermal thickness. In summary, EBN supplementation might increase bone strength and improve skin aging (as thinning of dermal layer is associated with skin aging in human subjects). The findings are in line with the ancient Chinese literature, in which EBN is believed to enhance skin complexion[16]. Through the study in Drosophila melanogaster, Hu et al., further described the anti-aging effect of EBN to be increasing the activity of antioxidant enzymes, fecundity and life span, and decreasing mortality rate and lipid peroxidation[17].

On top of that, investigation of EBN as a chondro-protective agent was carried out *in vitro* by using human articular chondrocytes that were isolated from knee joint of patients with osteoarthritis[18]. The addition of EBN to the cell cultures slows the progression of osteoarthritis and aided in the regeneration of cartilage. Moreover, EBN reduces catabolic activities and increases cartilage extracellular matrix synthesis. Hence, all these conditions would be helpful in alleviating osteoarthritis and hence it was speculated that EBN is a nutraceutical agent for the treatment of osteoarthritis.

Conclusion

Consumption of EBN has shown to bring multiple health benefits including antivirus, antioxidant and neuroprotection. It is also helpful in improving cardiometabolic diseases and bone degeneration. However many of these health effects were described in a handful of studies. More validation is required to not only confirm the findings but also to investigate the underlying mechanisms.

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