

Article

The Anti-Viral and Cognitive Enhancement Properties of Edible Bird's Nest: A Narrative Review

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ABSTRACT

Background: Edible bird's nest has been used as a traditional Chinese medicine since the 7th century. It is rich in protein, carbohydrates, moisture, ash, and fat. Recent research has focused on its potential health benefits, such as anti-viral properties, cognitive enhancement, and roles as an immunomodulator and antioxidant.

Objective: This review explores the anti-viral and cognitive enhancement properties of edible bird's nest.

Methods: This review followed the PRISMA Scoping Review (PRISMA ScR) guidelines. Relevant studies were systematically identified using PubMed and Google Scholar with keywords such as "edible bird's nest," "anti-viral," "cognitive enhancer," and "Alzheimer's disease." In vitro and in vivo studies published in peer-reviewed journals that focused on the anti-viral and cognitive effects of edible bird's nest were included. Articles were initially screened through titles and abstracts, and relevant studies were reviewed in full to extract key data on study design, methods, and outcomes.

Results: Edible bird's nest enhances cell functions by increasing the density and number of lysosomes, reducing Rab5 protein activity, enhancing mucin production, and modulating Rhoa expression, which regulates actin cytoskeleton dynamics. These mechanisms inhibit the attachment, endocytosis, maturation, and release of influenza A virus particles. As a cognitive enhancer, edible bird's nest significantly improves memory and neuroprotective functions by inhibiting neuroinflammatory processes and oxidative stress. Additionally, it may enhance mitochondrial function and increase the number of active mitochondria.

Conclusion: Edible bird's nest demonstrates anti-viral and cognitive enhancement effects with no reported side effects in vitro and in vivo. Further research should aim at clinical trials to establish effective and optimal dosages.

Keywords: Bird nest, Anti-viral, Cognitive, Enhancer

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INTRODUCTION

Edible bird's nest (EBN), also known as "Yan wo" or the "Caviar of the East," is a valuable natural resource with high nutritional content. It has been utilized in traditional medicine, particularly in China, since the 7th century (Loh et al., 2022). The demand for EBN continues to rise, with Indonesia serving as the largest exporter in Southeast Asia, exporting around 2,000 tons per year. China stands as the largest importer of EBN. In 2015, Indonesia's EBN exports reached 998 million US dollars and increased to 3.64 billion US dollars by 2019 (Chok et al., 2021).

EBN is rich in essential nutrients; however, its nutritional composition can vary due to several factors, including swallow species, habitat, harvest season, geographical location, and EBN grade. Generally, EBN contains significant levels of protein (42.0% - 63.0%), carbohydrates (10.63% - 27.26%), moisture (7.5% -

12.9%), ash (2.1% - 7.3%), and fat (0.14% - 1.28%) (Mohamad Nasir et al., 2021). Due to its diverse nutritional profile, EBN has been recognized for its potential health benefits, including anti-viral properties.

Previous research indicates that EBN may provide protection against viral infections, such as influenza A, a disease caused by a single-stranded RNA virus that can infect the respiratory tracts of birds, mammals, and humans (Chua et al., 2021). Effective control of influenza has been challenging due to the emergence of new viral strains, which delays the availability of influenza vaccines. Additionally, antiviral drugs face significant resistance issues. Studies have reported that EBN can neutralize and reduce viral titers without side effects (Guo et al., 2006; Haghani et al., 2017).

EBN contains sialic acid, which plays a role in neurological and cognitive functions in mammals. Sialic acid is involved in glycosidic bonds and forms N-acetylgalactosamine (GalNac), contributing to synapse maintenance and memory enhancement. Moreover, sialic acid supports cell repair, division, and proliferation. The concentration of sialic acid in the brain is linked to cognitive ability. Previous studies have shown that EBN improves cognitive function and increases the number of active mitochondria in the brain (Careena et al., 2018; Rashed et al., 2021). This literature review aims to summarize the potential of edible bird's nest as an anti-viral agent, cognitive enhancer, and its other health effects.

METHODS

Literature Search Strategy

The literature search was conducted on November 11, 2024, and was completed on the same day. The author systematically searched for relevant research articles using PubMed and Google Scholar. The search utilized a combination of keywords, including "edible bird's nest," "nutrition profile," "anti-viral," "cognitive enhancer," "immunomodulator," "antioxidant," "Alzheimer's disease," and "influenza A virus."

Selection Criteria

Inclusion criteria for this review consisted of original research papers published in English. The studies must focus on the health benefits of edible bird's nest, including its functions as an anti-viral agent and cognitive enhancer, encompassing in vitro, in vivo, and clinical research. Exclusion criteria included articles that were not available in full text and studies that did not discuss the health benefits of edible bird's nest.

Data Extraction and Categorization

Data extraction was performed independently by the author. Selected articles were thoroughly reviewed, and relevant information was extracted for analysis. The author recorded key study characteristics, such as the author(s), year of publication, study location, study design, and study duration. The extracted data were then organized into several themes, including the nutritional profile of edible bird's nest, its anti-viral effects, its cognitive enhancement effects, and other potential health effects of edible bird's nest. This systematic approach ensured a comprehensive overview of the existing literature.

RESULTS AND DISCUSSION

Overall Findings

The initial search yielded 256 records, with 116 remaining after removing duplicates. Following the screening of titles and abstracts, 39 studies were excluded, leaving 77 reports for further assessment of eligibility. Studies with irrelevant outcomes, those lacking full text, and non-English publications were excluded. Ultimately, this literature review included 23 studies.

Table 1. Anti-Viral Effect of Edible Bird's Nest

Author	Study Design	Doses	Result
Guo et al. 2006	In Vitro	0.5 - 4000 µg/ml	EBN containing <25 kDa protein mixed with pancreatin F showed the best potential in neutralizing the virus without adverse side effects. The highest concentration of 4 mg/ml did not cause any side effects.
Haghani et al. 2017	In Vitro	12.5 mg/ml	EBN with and without enzymatic treatment significantly reduced the virus titer with a protection level of 42% - 25%.

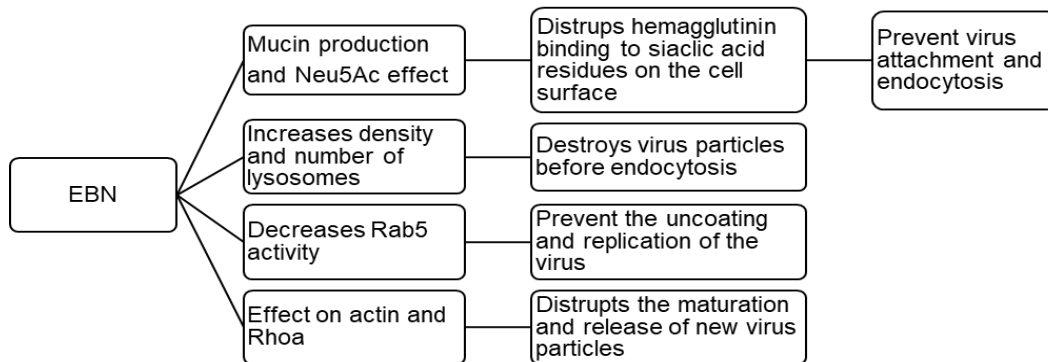


Figure 1. Mechanism of anti-viral effect of edible bird's nest

Edible Bird's Nest

Edible bird's nest (EBN), also known as "Yan wo" or the "Caviar of the East," is a valuable natural resource processed as a special food due to its high nutritional content. It has been used in traditional medicine, particularly in China, since the 7th century (Loh et al., 2022). EBN is found in several Southeast Asian countries, including Indonesia, Malaysia, Thailand, Myanmar, Vietnam, the Philippines, and Cambodia, as well as in southern China. As demand for EBN continues to rise, Indonesia remains the largest exporter in Southeast Asia, exporting around 2,000 tons per year, followed by Malaysia at 600 tons and Thailand at 400 tons. China is the largest importer of EBN. In 2015, EBN exports from Indonesia reached 998 million US dollars, further increasing to 3.64 billion US dollars by 2019 (Chok et al., 2021). EBN is derived from the saliva of swallows. Of the 24 species of swallows, only a few produce nests suitable for consumption, with the most common being *Aerodramus fuciphagus* and *Aerodramus maximus* (Hou et al., 2017). Swallows

construct 70-90% of their nests using their salivary secretions. Typically, EBN forms within about 35 days under optimal conditions of 90% humidity and temperatures between 28-30°C (Loh et al., 2022). While swallows originally build their nests in caves, increasing demand has led to the construction of specialized breeding houses that mimic their natural habitats (Tong et al., 2021).

Nutritional Profile of Edible Bird's Nest

The nutritional content of EBN can vary significantly based on several factors, including swallow species, habitat, harvest season, geographical location, and EBN grade. Generally, EBN contains high levels of protein (42.0% - 63.0%), carbohydrates (10.63% - 27.26%), moisture (7.5% - 12.9%), ash (2.1% - 7.3%), and fat (0.14% - 1.28%) (Mohamad Nasir et al., 2021). EBN contains nine essential amino acids—phenylalanine, valine, threonine, histidine, tryptophan, isoleucine, methionine, lysine, and leucine. Notably, lysine and tryptophan are only found in animal food sources, making EBN a valuable alternative for vegetarians. Essential amino acids are crucial for cell growth, development, regeneration, and the synthesis of neurotransmitters and antibodies. The concentration of essential amino acids in EBN (17.8 g/100 g) exceeds that of eggs (4.7-7.0 g/100 g) and milk (1.1 g/100 g) (Loh et al., 2022). Carbohydrates are the second most abundant component in EBN, constituting 27% to 58% of its composition. These carbohydrates include 9.0% sialic acid, 7.2% galactosamines, 5.3% glucosamine, 16.9% galactose, and 0.7% fructose. Sialic acid, a glycoprotein formed from chains of oligosaccharides and amino acids, plays a critical role in brain development, memory function, and learning ability (Rashed et al., 2021; Unal et al., 2022). Mineral content in EBN varies depending on the area of harvest. A study in Batu Pahat, Malaysia, revealed high concentrations of sodium (6109 mg/kg), magnesium (344 mg/kg), potassium (138 mg/kg), calcium (68 mg/kg), iron (4.52 mg/kg), chromium (0.3 mg/kg), selenium (0.14 mg/kg), and phosphorus (0.037 mg/kg). However, heavy metals such as zinc (1.2542 mg/kg), copper (0.6738 mg/kg), arsenic (0.0237 mg/kg), and lead (0.0203 mg/kg) were also present (Chok et al., 2021).

Factors Affecting the Nutritional Profile of Edible Bird's Nest

Studies indicate that *Aerodramus fuciphagus* has antioxidant properties and higher sialic acid content compared to *Aerodramus maximus*, which, due to its natural cave habitat, tends to produce nests rich in calcium and magnesium. The amino acid content of *Aerodramus fuciphagus* is reported to be 23% higher than that of *Aerodramus maximus* (Chok et al., 2021).

Geographical location is a significant factor influencing the nutrient composition of EBN. For instance, EBN from Thailand is noted for its high levels of sulfur-containing amino acids, calcium, and magnesium. Variations in fat content also exist across different regions, with EBN from Malaysia exhibiting the highest fat content, followed by Indonesia and Thailand. The dietary habits of the swallows, influenced by regional agricultural practices, affect this variation; for example, Thailand's extensive rice farming impacts the insects consumed by swallows, while Indonesia and Malaysia's oil palm plantations present another dietary source (Chok et al., 2021). Additionally, EBN samples from Thailand were found to lack proline, tryptophan, cysteine, and cystine, whereas some samples from Malaysia also did not contain proline and cystine (Daud et al., 2021). The rainy season is the optimal time for harvesting EBN, as the abundance of food for swallows during this period enhances the protein content of the nests. Research has shown that the highest protein levels are found in EBN harvested from December to March, although seasonal changes do not significantly affect mineral content (Chok et al., 2021).

The grade of EBN is determined by characteristics such as size, shape, color, and cleanliness. Research findings suggest that bowl-shaped nests have higher

protein and carbohydrate content and a greater level of cleanliness compared to stripe-shaped nests, as the former are composed mostly of mucin-rich glycoproteins (Mohamad Ibrahim et al., 2021). Different colors of swallows' nests also carry different qualities; for instance, white nests are predominantly made of saliva, while black nests may contain contaminants like feathers and dry leaves. Orange-red or brown-red nests, known as Xueyan or blood nests, are believed to absorb minerals, particularly sodium nitrite, leading to purportedly higher nutritional benefits, which also makes them more expensive (Lee et al., 2021).

Anti-Viral Effect of Edible Bird's Nest

Influenza A is a persistent disease that has caused numerous endemics and pandemics. Despite various efforts, including vaccinations and antiviral drugs, effective control remains elusive, especially when new strains emerge. Vaccination can only be developed several months after a pandemic begins, while antiviral drugs often face substantial resistance (Haghani et al., 2017). The Influenza A virus is a single-stranded RNA virus that primarily infects the respiratory tracts of birds, mammals, and humans. It is characterized by two key surface proteins: hemagglutinin (HA), which binds to sialic acid on the surface of respiratory epithelial cells, and neuraminidase (NA), which cleaves sialic acid to facilitate viral entry into host cells. After entering a host cell, the virus undergoes conformational changes that release its genetic material, leading to replication and the production of new viral particles (Chua et al., 2021; Kalil & Thomas, 2019).

Research by Haghani et al. (2017) demonstrated that EBN increased the density and number of lysosomes in both infected and uninfected cells, aiding in virus destruction. Additionally, EBN reduced the activity of Rab5 protein, which is vital for endocytosis and vesicular transport, while modulating RhoA expression to enhance actin cytoskeleton dynamics. This modulation minimizes cellular damage from viral infections and prevents the maturation and release of new viral particles. Comparisons between EBN with and without enzymatic treatment reveal that untreated EBN decreased neuraminidase copy number and NS1 expression outside the cell but increased NS1 expression inside the cell. Conversely, EBN treated with pancreatin F enzyme resulted in increased neuraminidase copies inside the cell, NS1 expression outside the cell, and M2 expression inside the cell, indicating a greater capability to inhibit viral material release (Haghani et al., 2017).

Another study confirmed that enzymatic treatment of EBN significantly enhances its effectiveness against influenza infection. The sialic acid present in EBN contains Neu5Ac residues that disrupt the ability of viral hemagglutinin to bind with sialic acid receptors on host cells. The treatment with Pancreatin F reduces EBN protein size to smaller fragments (10-25 kDa), which enhances the inhibitory effect of Neu5Ac residues. Higher doses of EBN significantly decreased hemagglutinin activity in influenza A virus, with increased doses correlating with greater inhibitory effects. Moreover, EBN promotes mucin production, which serves as a physical barrier, preventing hemagglutinin from binding to sialic acid on the host cell surface; without this binding, the virus cannot enter the cell (Chua et al., 2021).

Cognitive Enhancer Effect of Edible Bird's Nest

The brain is one of the most complex and vital organs in humans, and its aging process is characterized by decreased size and a decline in neurotransmitter systems. Alzheimer's disease, a common neurodegenerative disorder, currently affects approximately 44 million individuals worldwide, with predictions suggesting that by 2050, 1 in 85 people will be afflicted (Rashed et al., 2021; W. Wang et al., 2020). Multiple factors contribute to Alzheimer's development, including age, gender, weight, lifestyle, toxins, brain injury, and genetic mutations. The mechanisms underlying Alzheimer's disease remain inadequately understood.

Some studies suggest a correlation between Alzheimer's and mitochondrial damage. Mitochondria in neurons are crucial for energy production, calcium regulation, and neurotransmitter synthesis. Damage to these organelles impairs glucose and energy metabolism, particularly in areas critical for memory and cognitive function, such as the cortex and hippocampus. This damage leads to oxidative stress, which further harms mitochondrial DNA (mtDNA) and accelerates Alzheimer's progression (W. Wang et al., 2020).

EBN contains sialic acid, which significantly impacts neurological and cognitive functions in mammals. Sialic acid is present in glycosidic bonds and forms N-acetylgalactosamine (GalNac), which helps maintain synaptic function and enhances memory performance (Careena et al., 2018). Furthermore, sialic acid aids in cellular repair, division, and proliferation. Variations in the concentration of sialic acid in the brain are linked to cognitive abilities. Research in rats indicates that sialic acid supplementation can boost brain ganglioside concentrations, which are vital for cognitive performance (Rashed et al., 2021). In a study by Careena et al. (2018), mice were administered lipopolysaccharide (LPS), a component of gram-negative bacteria that triggers oxidative stress and neuroinflammation resembling Alzheimer's disease. The LPS-treated mice exhibited diminished cognitive function and memory, alongside increased levels of pro-inflammatory cytokines (TNF- α , IL-1 β , and IL-6) in the hippocampus. However, when these rats were pre-treated with EBN prior to LPS administration, there was a notable reduction in pro-inflammatory cytokine production. As a result, they performed better in the Y-maze test, demonstrating improved spatial memory without significant side effects. This study suggests that EBN pretreatment substantially enhances memory and neuroprotective function by inhibiting neuroinflammatory processes and oxidative stress. Another study by Rashed et al. (2021) employed the mitochondrial membrane potential (MtMP) technique to investigate whether sialic acid contributes to mitochondrial health. SH-SY5Y neuroblastoma cells, which closely resemble normal nerve cells, were used for this research. The findings indicated that EBN has the potential to improve mitochondrial function and increase the number of active mitochondria within these cells.

Table 2. Cognitive Enhancer Effect of Edible Bird's Nest

Author	Study Design	Doses	Result
Careena et al. 2018	In Vivo	125, 250, and 500 mg/kg	EBN pre-treatment was shown to improve cognitive function and memory without significant side effects.
Rashed et al. 2021	In Vitro	20, 40, 60, 80 and 100 μ g/ml	EBN can repair and increase the number of active mitochondria with a dose of \leq 60 μ g/ml is a safe dose.

Other Effect of Edible Bird's Nest

Prior research has also reported that EBN possesses immunomodulatory benefits. In vivo studies involving mice subjected to chemotherapy with cyclophosphamide (CY), which typically causes damage to healthy cells and reduces immunity, showed promising results with EBN administration. Specifically, EBN was found to enhance B cell growth and restore the balance of CD3+ T cells and CD19+ B cells. In addition, EBN increased IgA and IgG3 secretion, highlighting its crucial role in the humoral immune response (Zhao et al., 2016).

Furthermore, EBN has demonstrated protective effects against UVB radiation, which can induce oxidative stress and photoaging of the skin. Exposure to UVB

radiation causes excessive production of reactive oxygen species (ROS), leading to wrinkles, increased melanin production, and decreased hyaluronic acid levels in keratinocytes. EBN has been shown to boost hyaluronic acid synthesis and repress melanogenesis, making it a beneficial supplement for photoaging prevention (Kim et al., 2021). Supporting evidence from a study by Masuda et al. (2022) indicated that rats exposed to UVB radiation for 10 weeks and subsequently administered EBN (20 mg/kg/day) exhibited reduced skin damage from UV exposure. This study suggests that a human dosage of 1-2 grams per day may yield similar protective results (Masuda et al., 2022).

Safety of Edible Bird's Nest

While EBN offers numerous health benefits, it is essential to consider potential contaminations, including excessive nitrite, nitrate, heavy metals, mold, bacteria, and pests. Contamination can occur throughout the cultivation, processing, storage, and shipping stages of EBN. Generally, EBN harvested from caves exhibits higher levels of contamination compared to that from swallow houses, likely due to better ventilation and hygiene at the latter sites. Historically, there were instances where EBN exported from Indonesia and Malaysia to China had critically high nitrite levels (11,000 ppm), prompting a halt in exports until regulations were enforced. The World Health Organization (WHO) establishes a permissible daily intake of nitrite at 0 - 3.7 mg/kg body weight. In the body, nitrite can convert to nitric oxide, which may cause vasodilation and lower blood pressure. Additionally, nitrite can react with amino acids to form nitrosamines, a class of carcinogenic compounds that can develop during cooking at high temperatures (Yeo et al., 2021).

The levels of nitrite and nitrate in EBN can be influenced by environmental factors such as humidity, pH, climate, and cleaning procedures. Moreover, heavy metals like arsenic and lead are of concern, particularly in EBN obtained from swallow houses where contamination can occur from rusty iron or polluted water sources. A previous study conducted in Malaysia found no contamination from harmful bacteria; however, fungal contamination was identified due to high humidity, posing a health risk, especially for individuals with weakened immune systems (Tan et al., 2020). To mitigate contamination risk, Indonesia and Malaysia established Standard Operating Procedures (SOPs) for EBN exports in August 2011, ensuring that all exported EBN complies with strict safety standards (Yeo et al., 2021).

Weakness of Edible Bird's Nest

Despite its many advantages, EBN has several weaknesses. The nutritional content and quality of EBN can vary based on factors such as swallow species, habitat, harvest season, geographical location, and grading criteria. The rising market demand for EBN has led to price increases, with costs ranging from 1,000 to 10,000 US dollars per kilogram, making it unaffordable for many (Chok et al., 2021). Additionally, there are cases of EBN products being adulterated with ingredients such as pig skin, tremella mushroom (*Tremella fuciformis*), starch, agar, egg white, and karaya gum (*Sterculia urens*). A common adulterant is red seaweed, which can trigger allergic reactions in sensitive individuals. These mixtures often diminish the quality and nutritional content of EBN compared to pure products. Concerns regarding halal compliance also arise with the addition of pork-derived components, which are unsuitable for Muslim consumers (Chok et al., 2021; X. Wang et al., 2023).

CONCLUSION

EBN exhibits anti-viral and cognitive enhancement effects without associated side effects, as evidenced by both in vitro and in vivo studies. However, the current research predominantly emphasizes the bioactive components of EBN and their potential benefits based on animal studies and laboratory models. To date, there

have been no clinical trials conducted to establish the optimal or specific dosage for human use. Therefore, future research should prioritize conducting clinical trials to definitively determine the effective and optimal dosage of edible bird's nest for its anti-viral and cognitive enhancement properties.

CONFLICT OF INTEREST

Author(s) stated that there is no conflict of interest.

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