Exploring the therapeutic potential of *Nigella sativa* (Habbatusauda) in Autism spectrum disorder :

A comprehensive analysis of benefit and mechanism.

Dr. Mustafa Ali Mohd. *FASc*
MALAYSIA

NIGELLA SATIVA

Nigella sativa is a herb which has been used as medicine for hundreds of years by communities around the globe for various medicinal purposes.

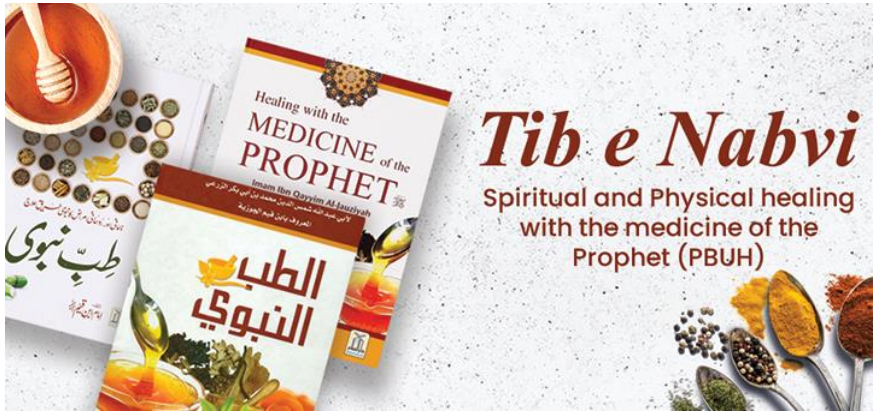
Goodness of *Nigella sativa* is NOT NEW

- In Islamic literature: one of the greatest forms of therapeutics.
- Avicenna's "Canon of Medicine" : Nigella Sativa seed can lessen weakness and depression and improve the body's vitality.
- This plant has been included in the list of natural medications in different medicines including Tibb-e-Nabavi (The medication of Prophet Mohammad),

Nigella sativa has been widely investigated for its biological activities and restorative potential and demonstrated to have a wide range of activities:

diuretic,
antihypertensive,
anti-diabetic,
anti-cancer,
immune-modulatory,
antimicrobial,
anthelmintic,
analgesics

bronchodilator,
antiinflammatory,
anti-tussive,
gastro-protective,
hepato-protective,
decreasing LDL cholesterol,
renal- protective
anti-oxidant properties



PHYTOCHEMICAL CONSTITUENTS OF *Nigella sativa*

Quinones

Thymoquinone
Dithymoqionone
Thymohydroquinone

Pyrazole Alkaloids

Nigellidine
Nigellicine

Isoquinoline Alkaloids

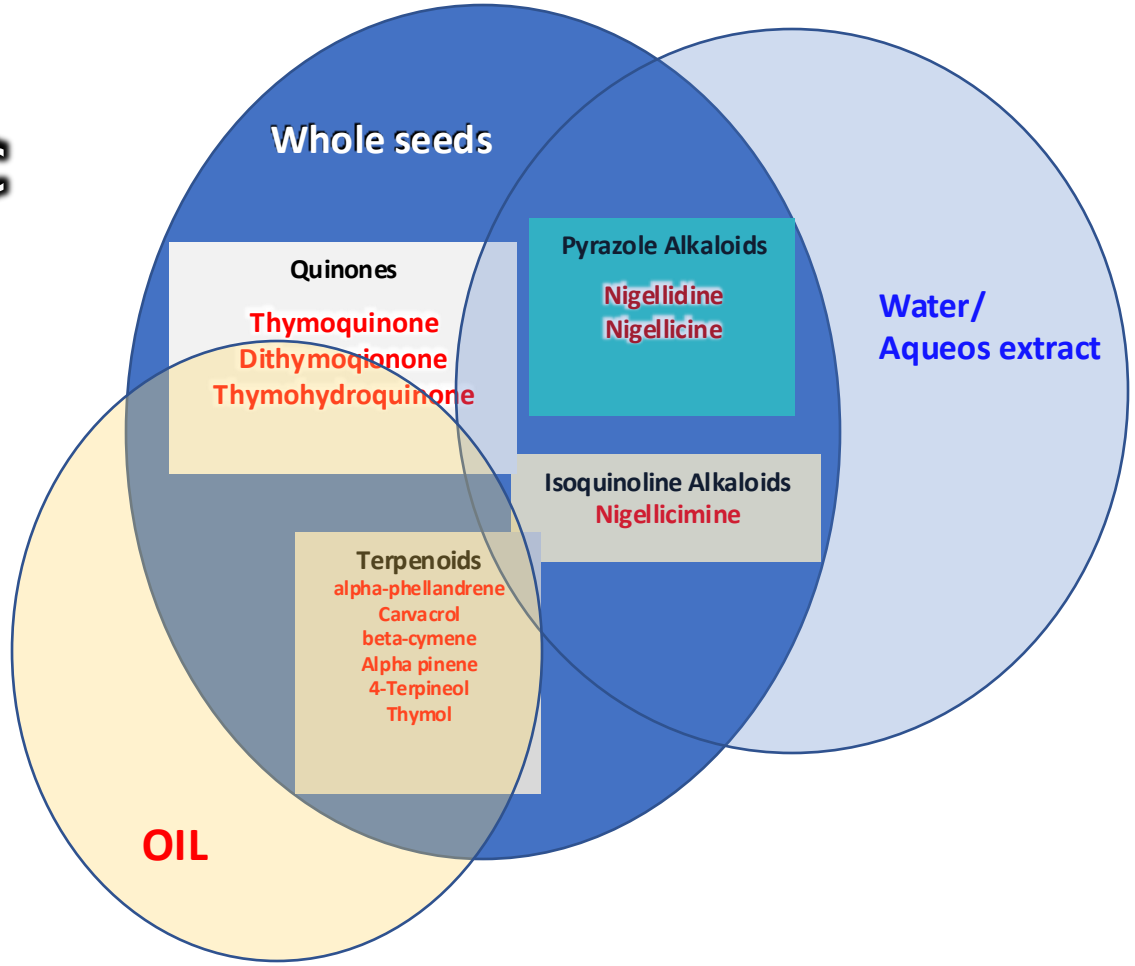
Nigellicimine

Terpenoids

alpha-phellandrene
Carvacrol
beta-cymene
Alpha pinene
4-Terpineol
Thymol

Habbatusauda requires a specific formulation to provide optimal effects. The most commonly available Habbatusauda product on the market is Habbatusauda oil."

Habbatusauda requires a specific formulation. It should contain 100% *Nigella sativa* content



Habbatusauda oil does not contain a complete 100 percent composition. It only includes substances that are soluble in oil. Other components do not enter into this Habbatusauda oil. Therefore, it is not complete."

Another form of Habbatusauda product is in the form of a water extract. This is also incomplete because it only contains substances that are soluble in water. We will not get the full effect of Habbatusauda."

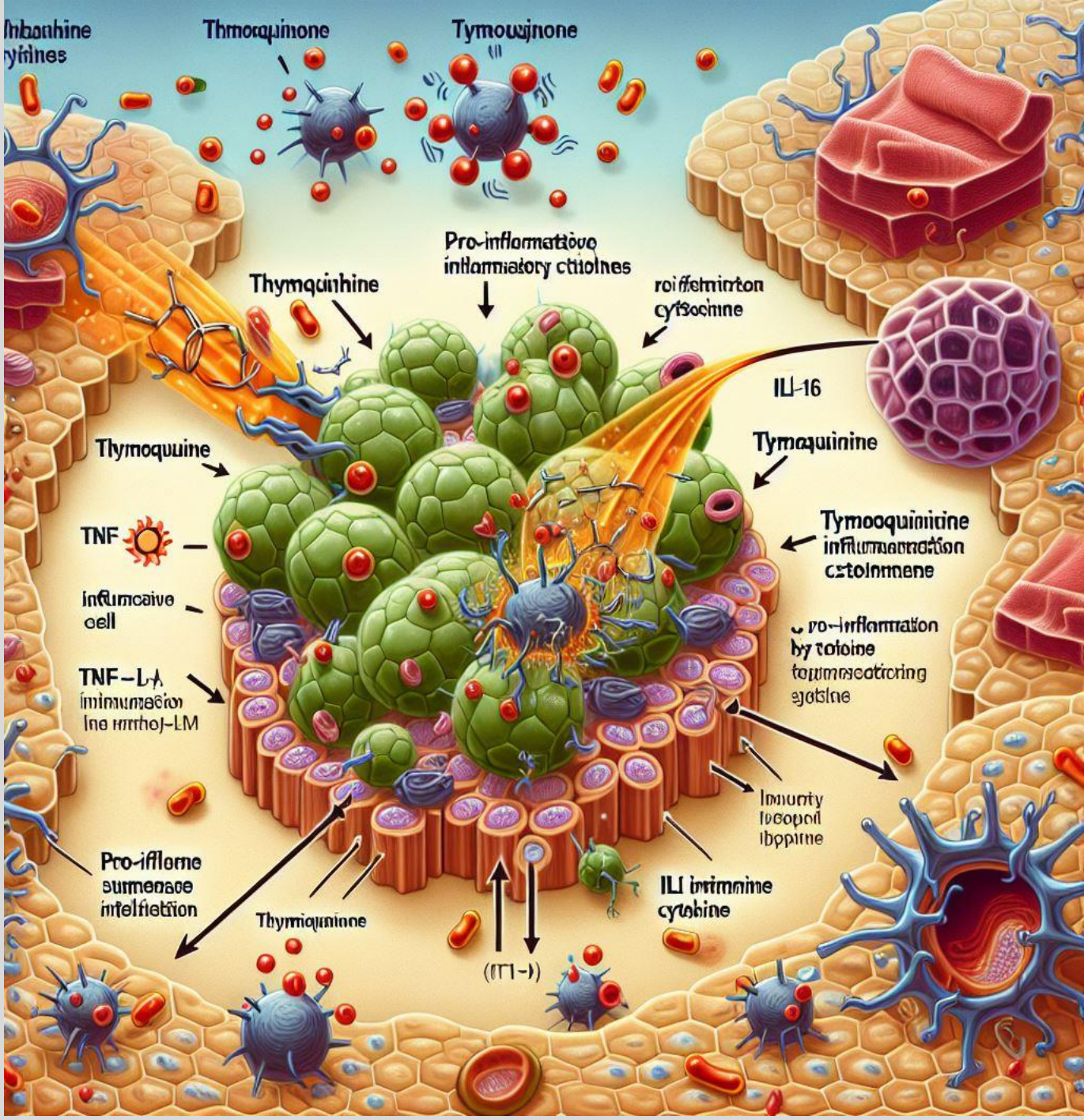
"Some people consume Habbatusauda by chewing the seeds. This is also not perfect because the seeds are very hard and not easily fully absorbed by the intestines. Therefore, what is obtained in this way does not provide us with 100% of the Habbatusauda content."


Thymoquinone,
the main active ingredient of *Nigella sativa*.
Antioxidant, hepatoprotective
Anti-inflammatory,
Immunomodulatory
Hypercholesterol, Diabetes, Gout
Rhinitis, Cough, Halitosis,
Antiviral, Energy booster,
Hypertension,
Anticoagulant.

Thymoquinone exhibits significant anti-inflammatory properties through several mechanisms:

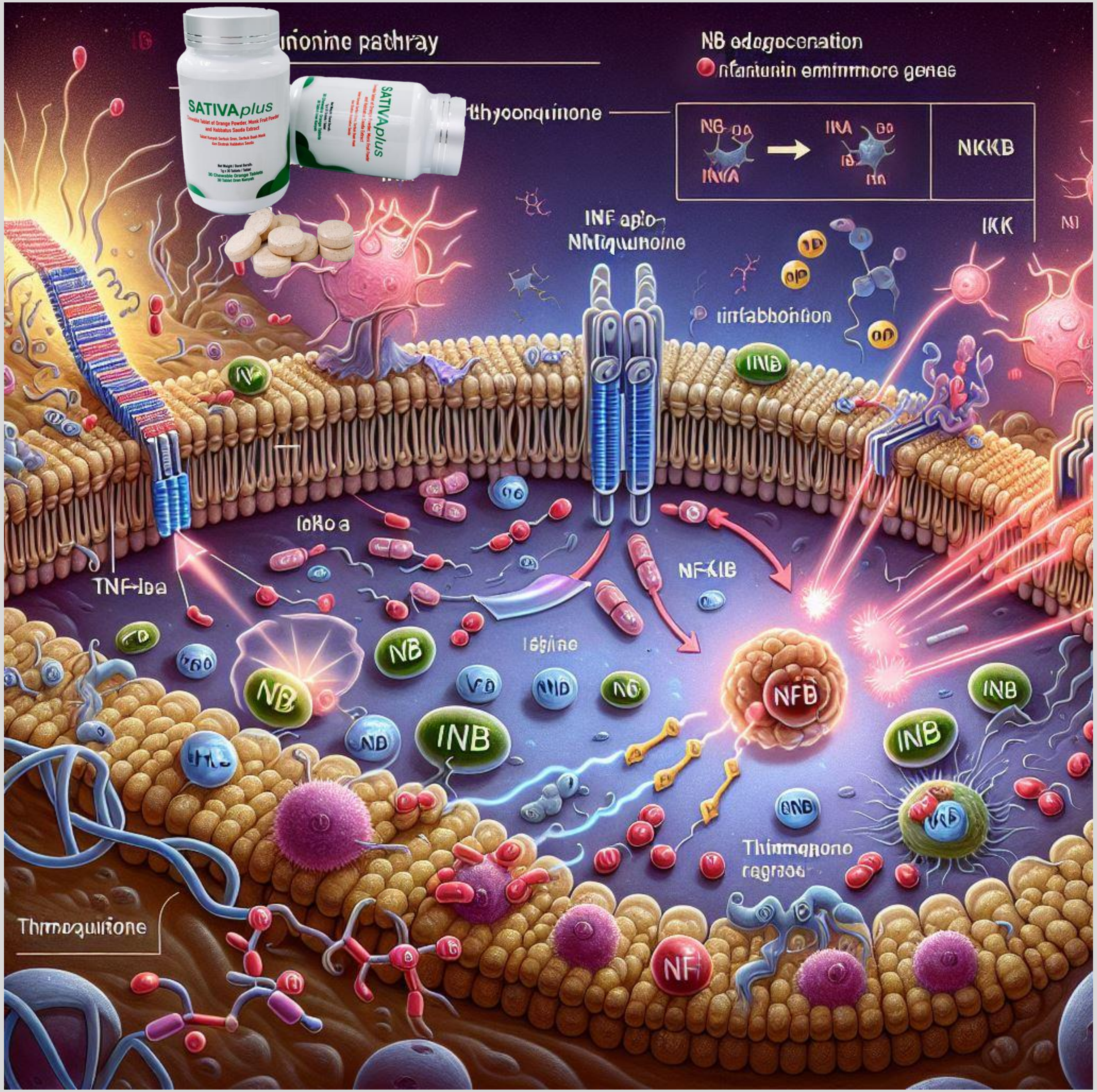
Inhibition of Inflammatory Cytokines:

Thymoquinone suppresses the production of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, which are key players in the inflammatory response

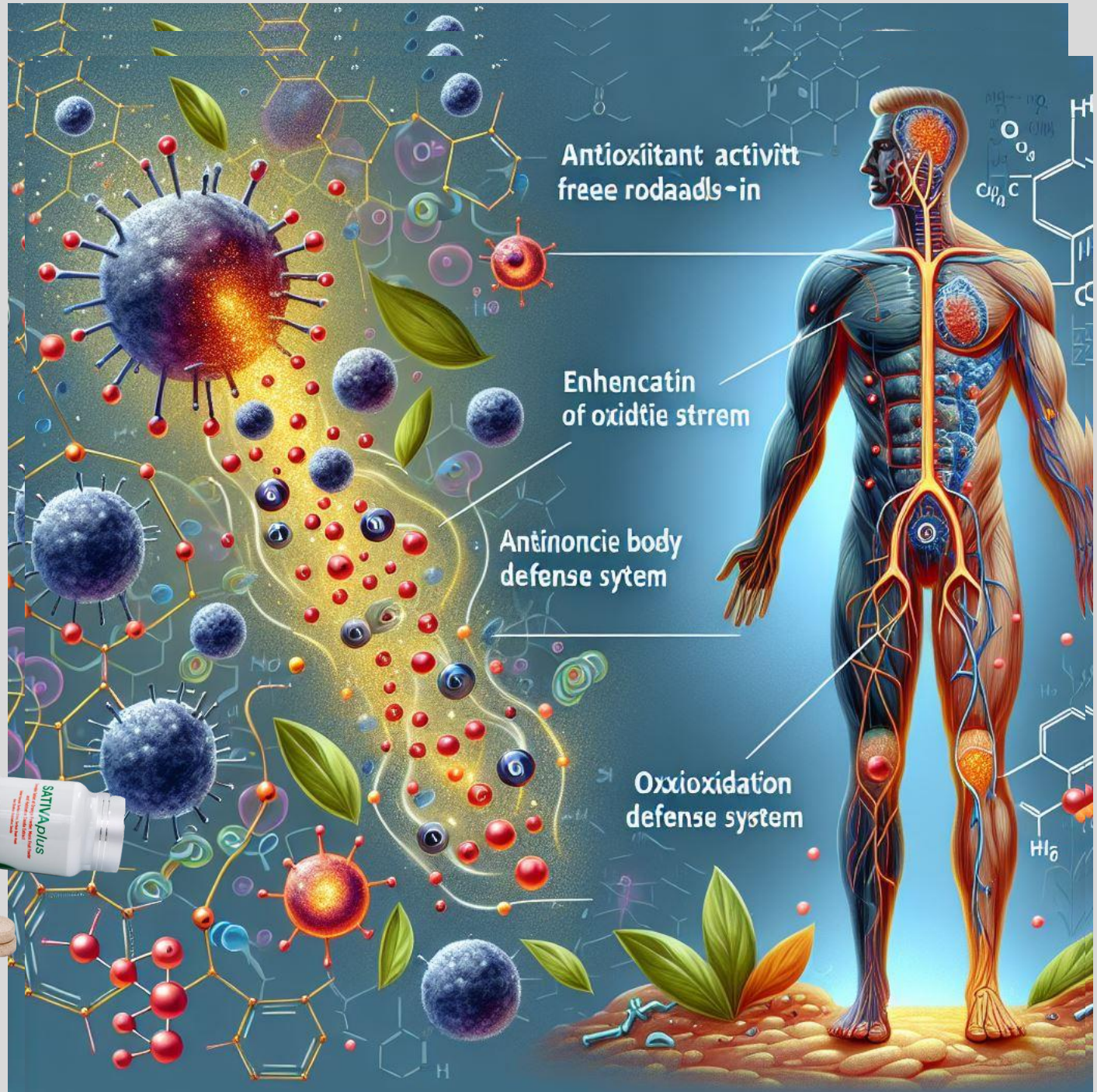


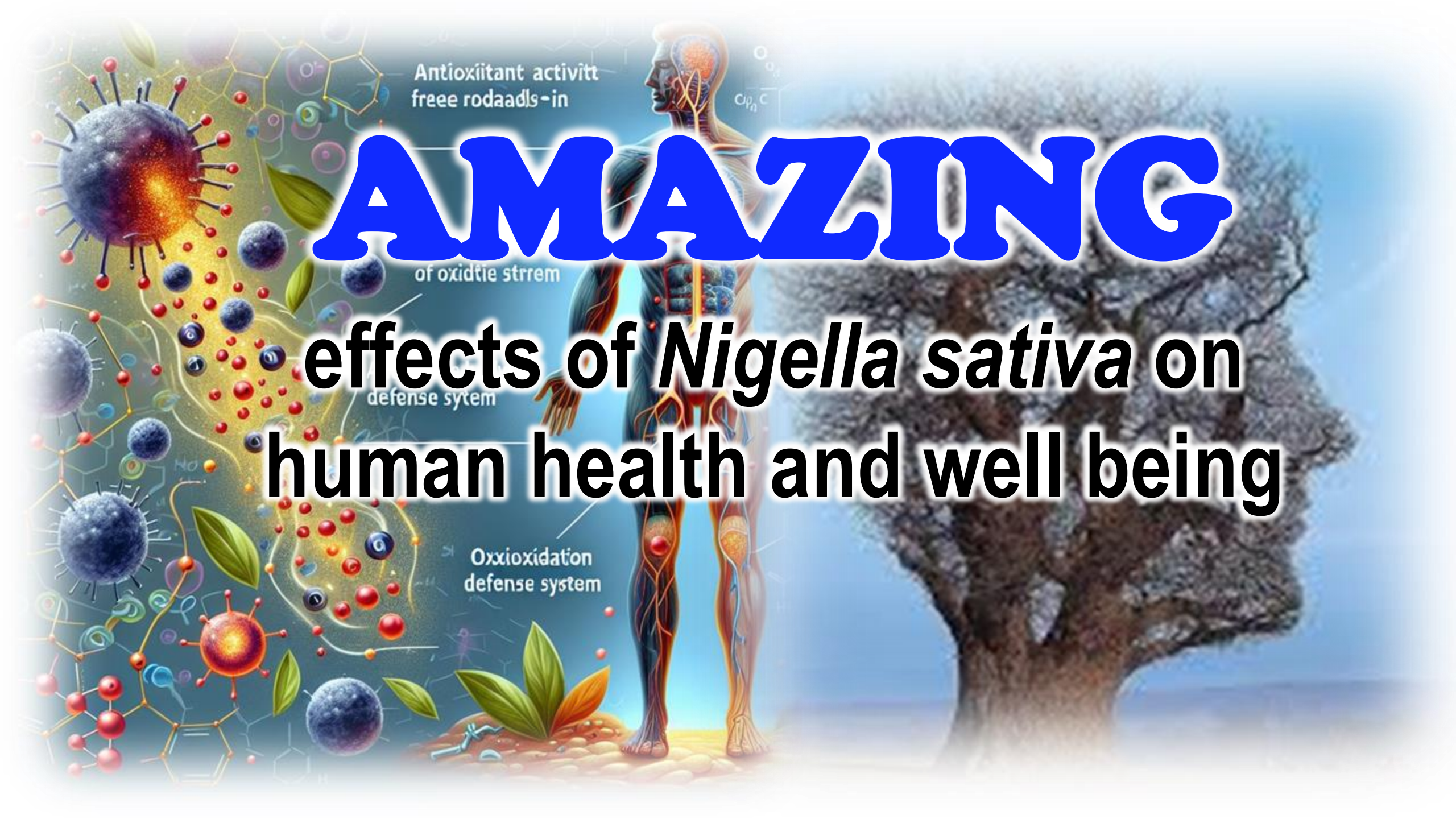
Modulation of Enzymatic Pathways:
It inhibits the activity of enzymes like cyclooxygenase (COX) and lipoxygenase (5-LO), which are involved in the synthesis of inflammatory mediators such as prostaglandins and leukotrienes

Suppression of NF-κB Pathway: Thymoquinone inhibits the activation of NF-κB, a transcription factor that regulates the expression of various inflammatory genes



Antioxidant Activity: By scavenging free radicals and enhancing the body's antioxidant defense system, thymoquinone reduces oxidative stress, which is closely linked to inflammation

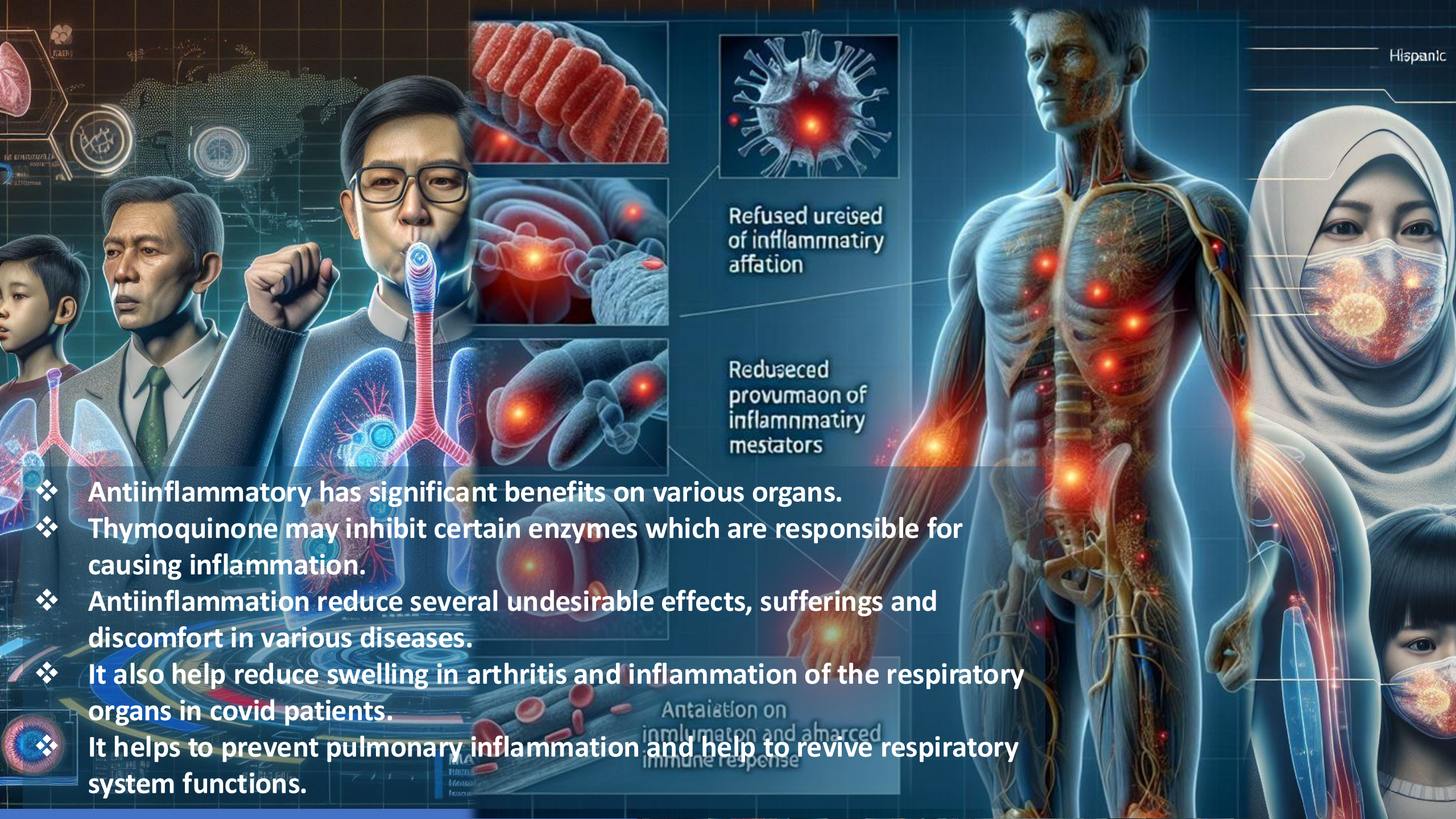




AMAZING

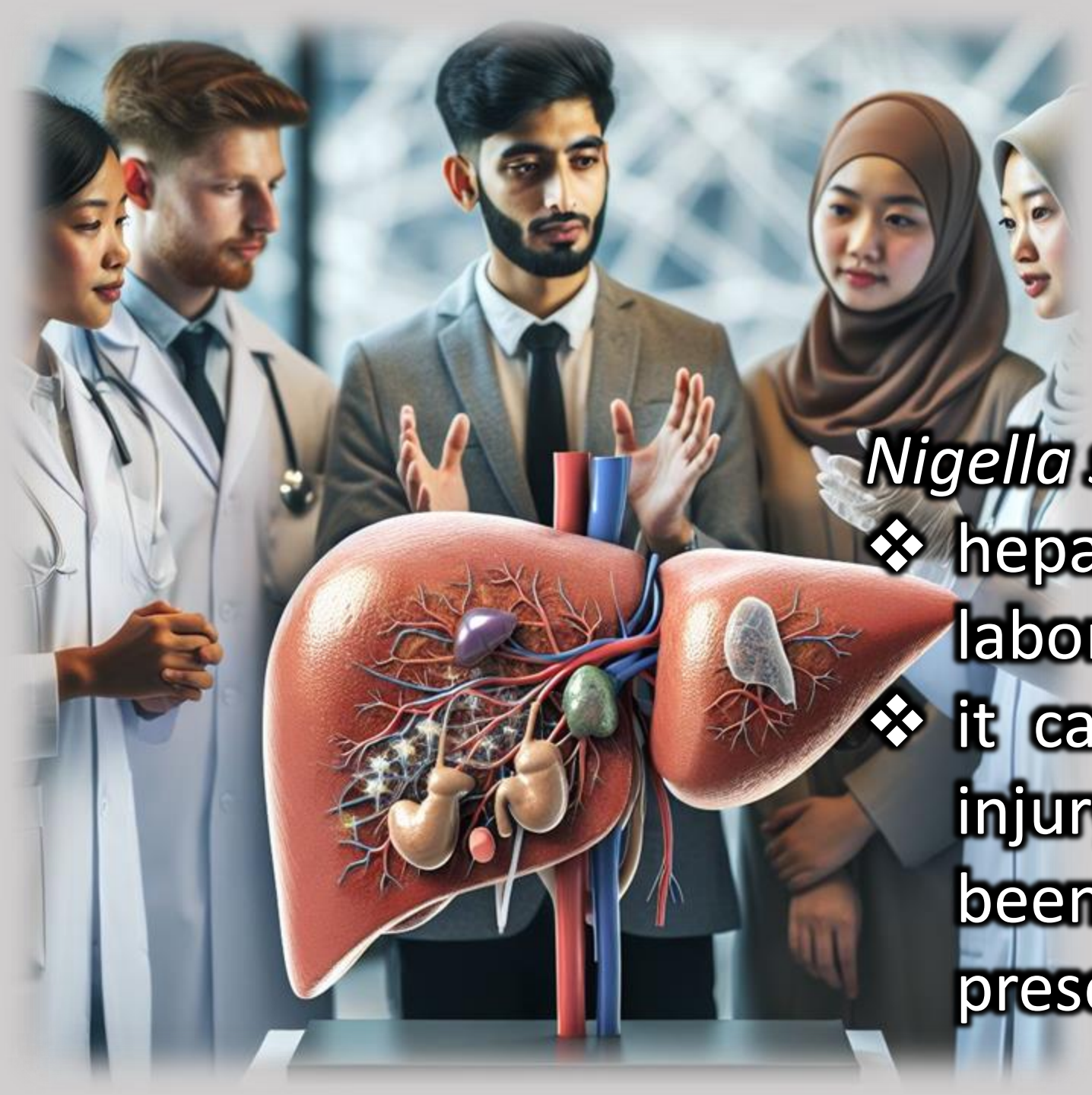
effects of *Nigella sativa* on human health and well being

Nigella sativa has antiinflammatory effects



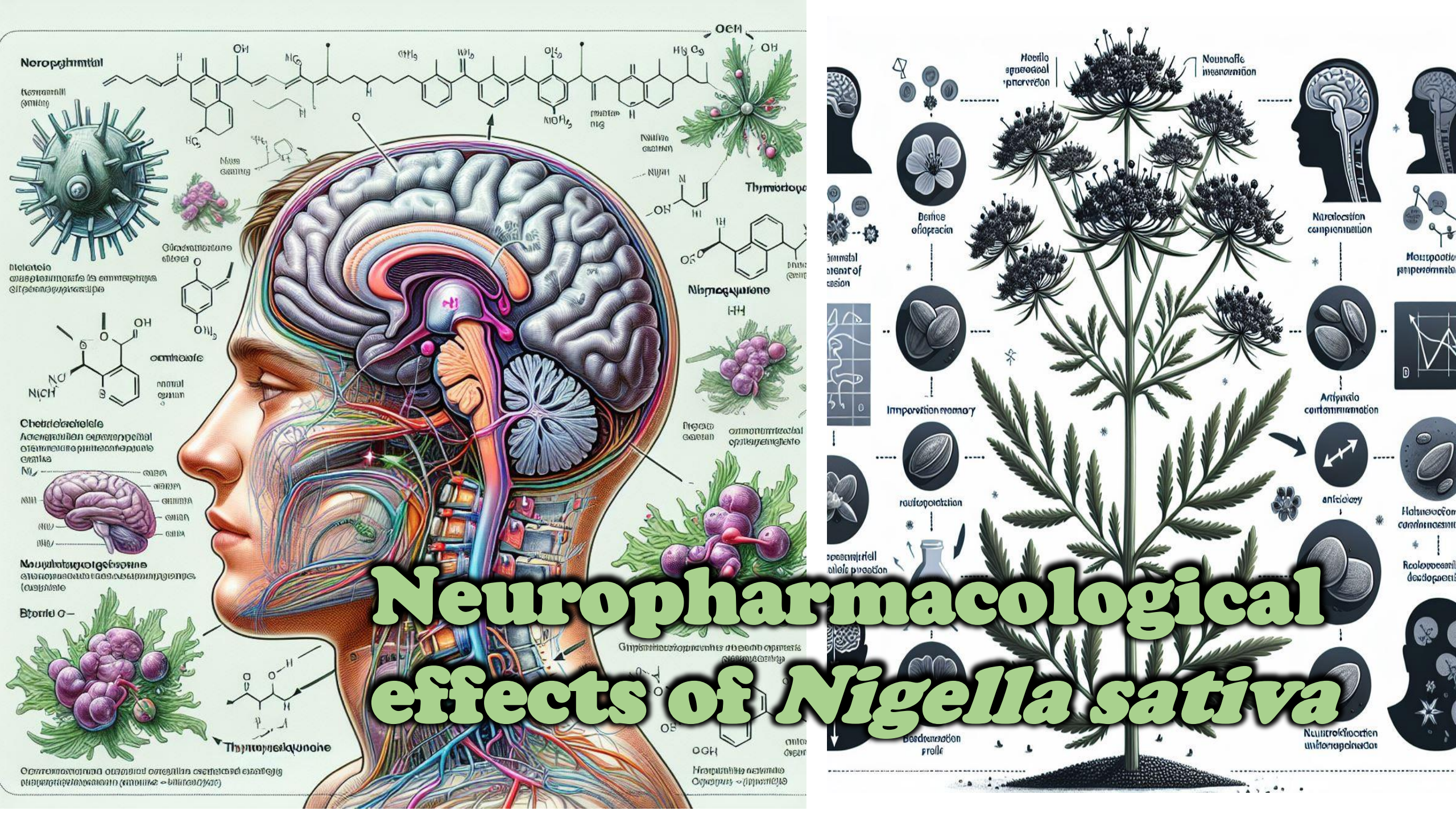
- Antiinflammatory has significant benefits on various organs.
- Thymoquinone may inhibit certain enzymes which are responsible for causing inflammation.
- Antiinflammation reduce several undesirable effects, sufferings and discomfort in various diseases.
- It also help reduce swelling in arthritis and inflammation of the respiratory organs in covid patients.
- It helps to prevent pulmonary inflammation and help to revive respiratory system functions.

Nigella sativa has hepatoprotective effects



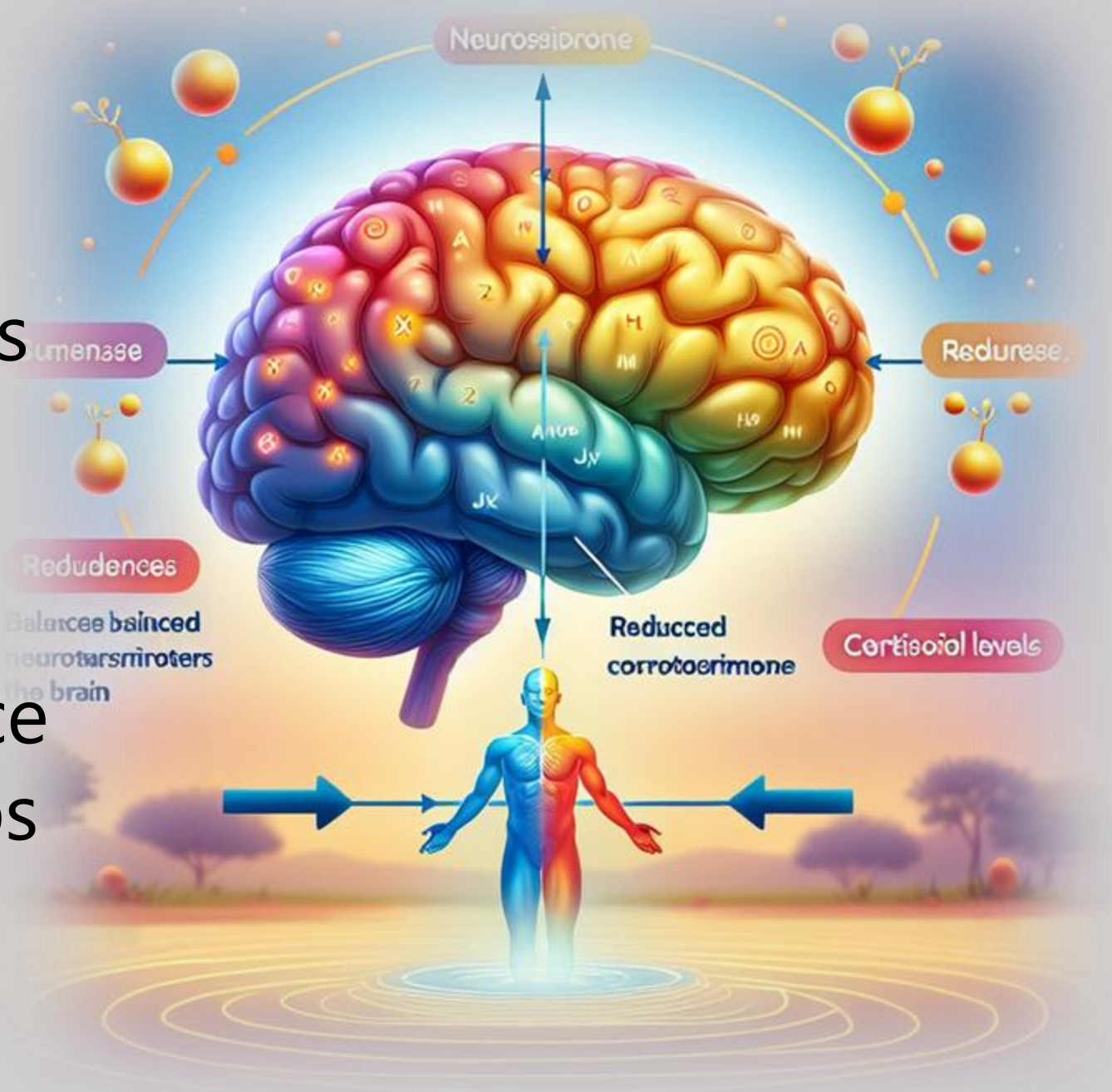
Nigella sativa:

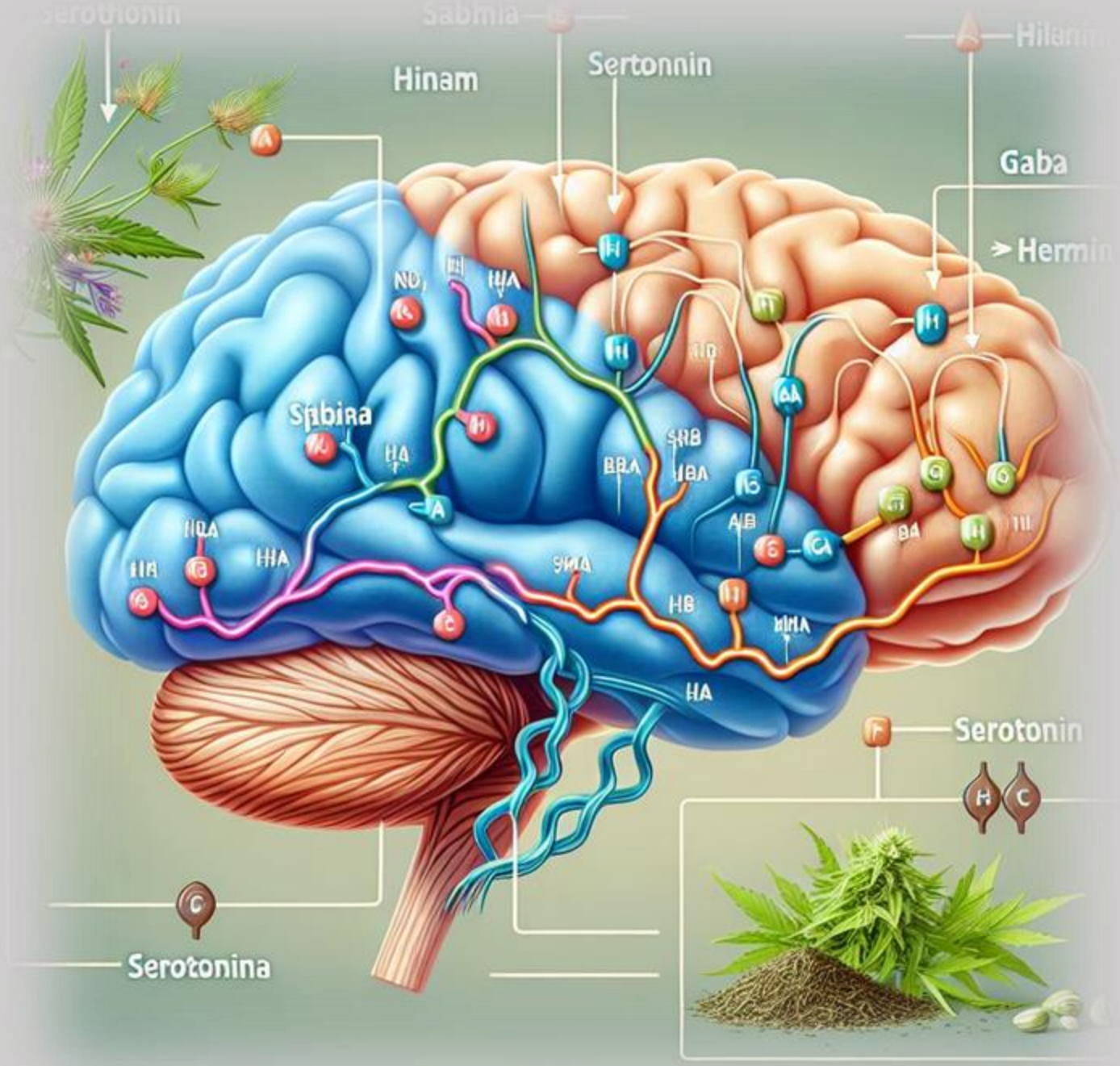
- hepatoprotective effects on laboratory animals,
- it can protect the liver from injury or toxins. This effect has been shown to be due to the presence of thymoquinone.


Neuropharmacological
effects of Nigella sativa


Nigella sativa has
anti anxiety effect

Thymoquinone:
It has been shown to balance neurotransmitters in the brain, similar to some anti-anxiety medications.
Thymoquinone can reduce cortisol levels, which helps lower the body's stress response.



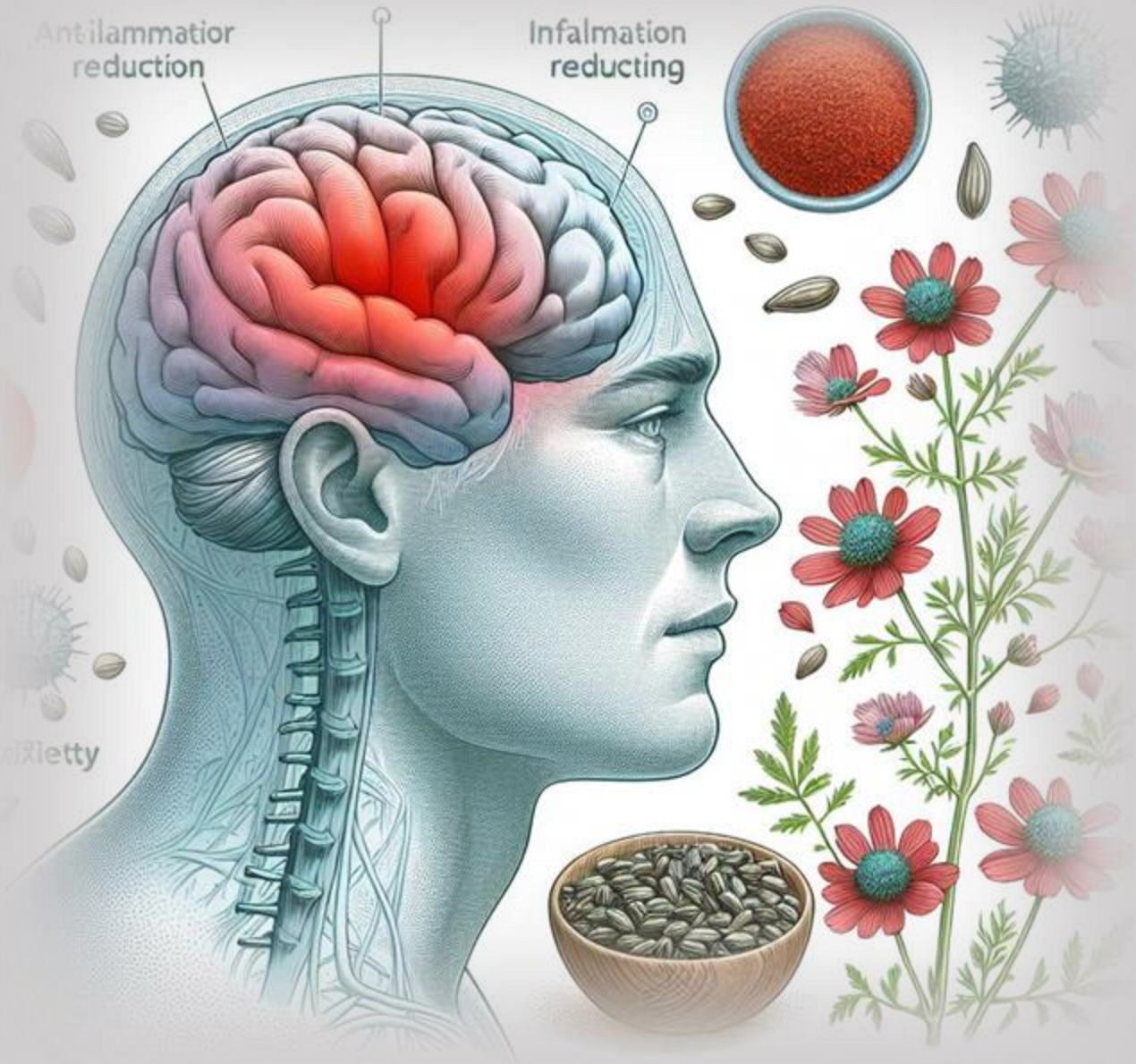


Serotonin and GABA Pathways:

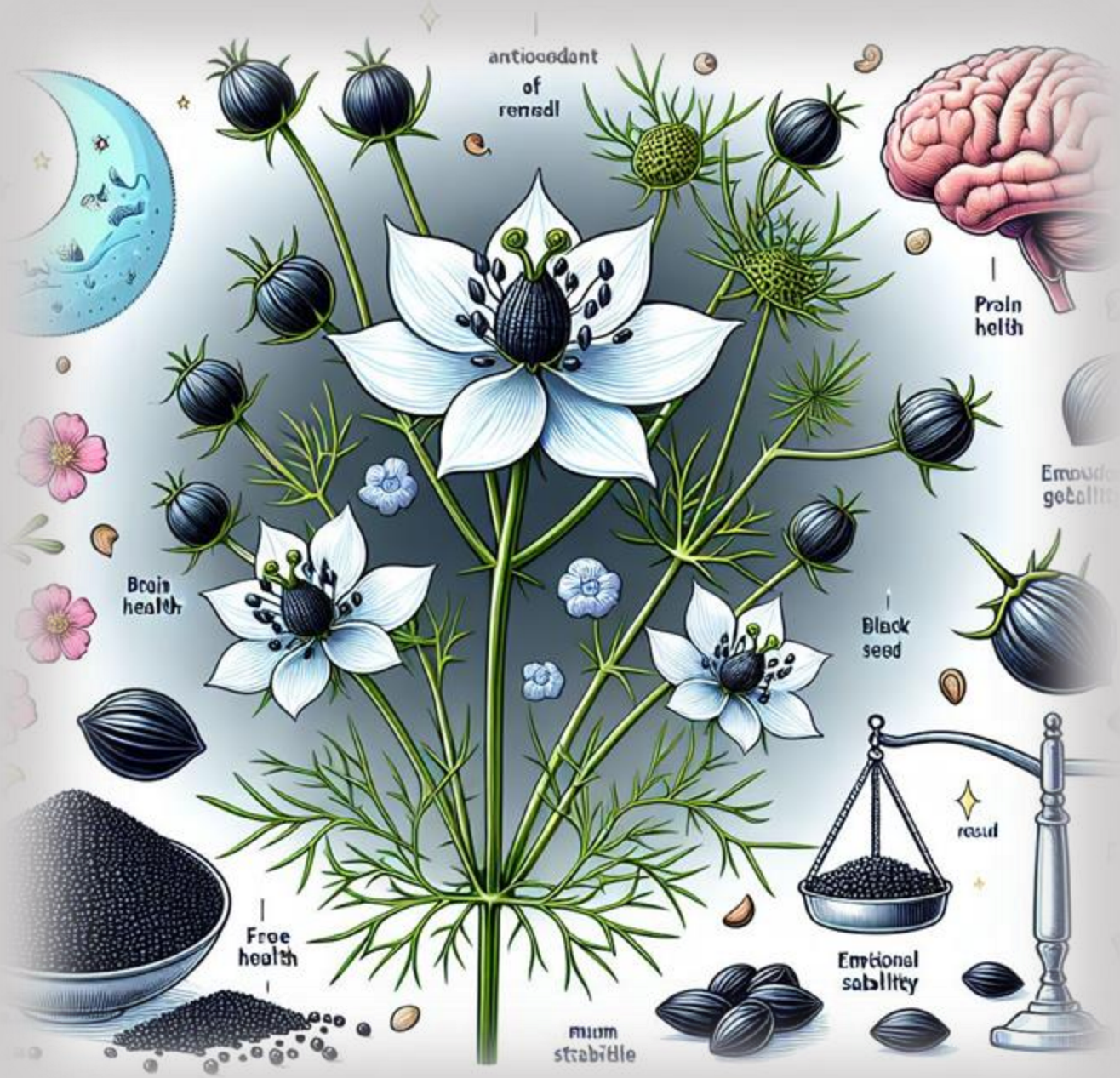
Nigella sativa may increase serotonin levels and enhance GABA activity.

Both serotonin and GABA are crucial for maintaining mood stability and promoting relaxation.

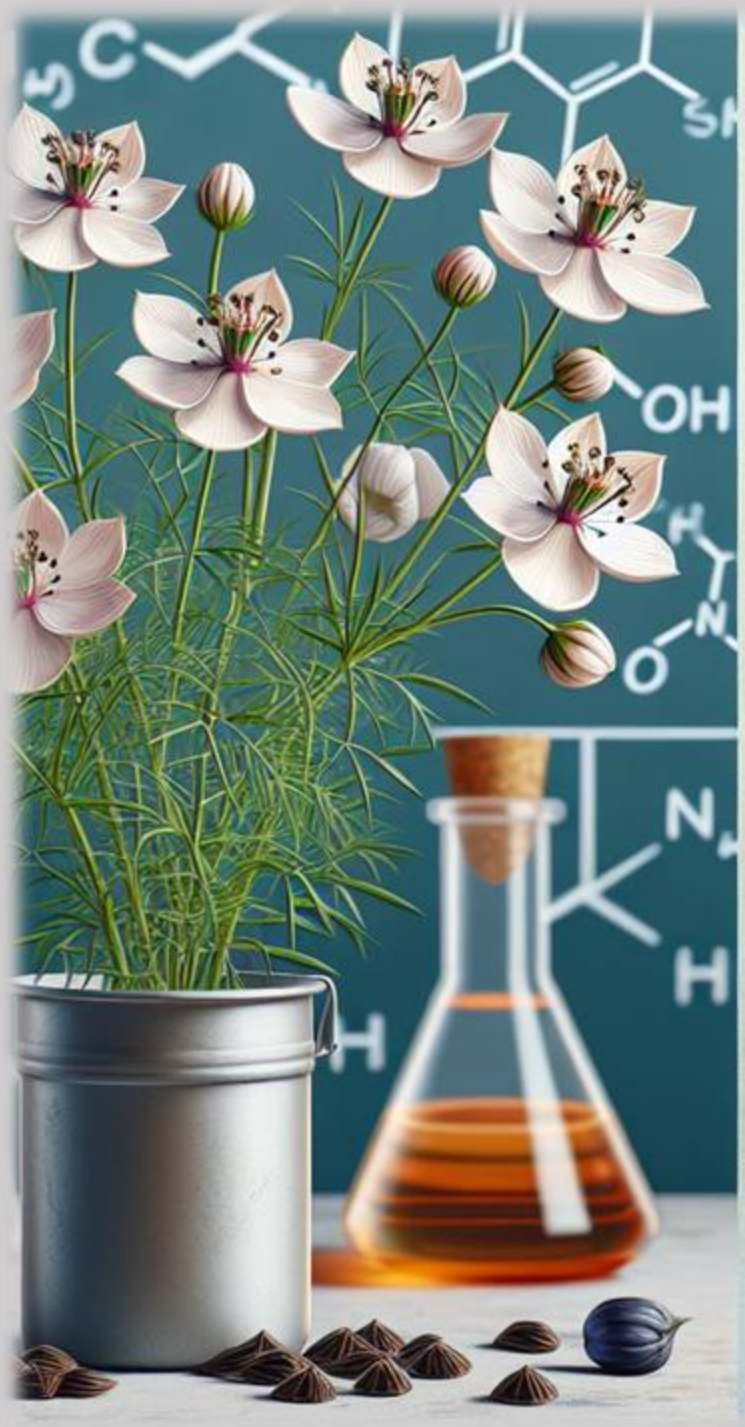
Anti-inflammatory Effects: Chronic inflammation is associated with anxiety and other mental health issues. Nigella sativa's anti-inflammatory properties help reduce inflammation markers, contributing to its anxiolytic (anxiety-reducing) effects



Antioxidant Properties: Nigella sativa is rich in antioxidants, which combat oxidative stress. Oxidative stress is linked to anxiety and other mental health conditions. By neutralizing free radicals, Nigella sativa supports better brain health and emotional stability



Nigella sativa, Neurotoxicity and Neurodegeneration



Neurotoxicity: harm to the brain or peripheral nervous system caused by exposure to natural or man-made toxic substances.

These poisons can affect the nervous system and can upset or kill the neurons.

amyloid β peptide (Aβ)

α-synuclein

Environmental toxins

Food and drinks

Amyloid beta peptide (Aβ)

Amyloid beta peptide (Aβ) is a protein fragment derived from a larger protein called amyloid precursor protein (APP).
In Alzheimer's disease, it forms the core component of amyloid plaques found in the brains of affected individuals.

- **Formation**: Aβ is produced when APP is cleaved by enzymes called beta-secretase and gamma-secretase1

- **Function:** Normal function is not fully understood, Aβ is believed to be involved in processes like activating kinase enzymes, protecting against oxidative stress, and regulating cholesterol transport

- **Pathology:** In Alzheimer's disease, Aβ aggregates to form plaques that disrupt cell function and are toxic to neurons

Thymoquinone can prevent neurotoxicity and amyloid-beta-induced apoptosis.

Amyloid beta peptide (Aβ)

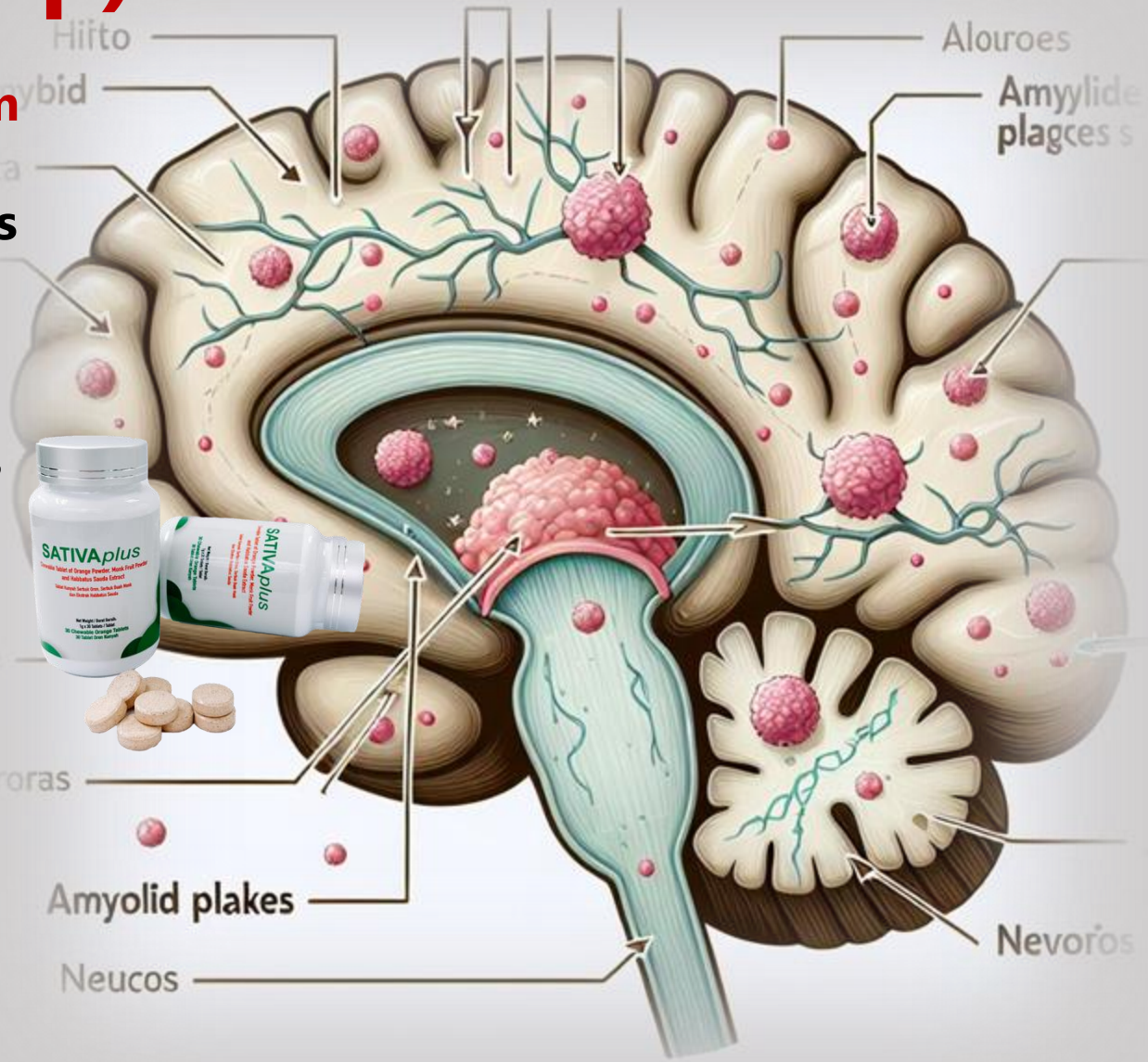
Research has shown that individuals with **autism** may have altered metabolism of amyloid precursor protein (APP), leading to higher levels of certain APP metabolites and amyloid beta peptides in the brain.

\

Oxidative Stress: The presence of Aβ in neurons is associated with increased oxidative stress, which can contribute to neuronal damage.

APP Metabolism: Altered APP metabolism has been observed, with higher levels of secreted APP (sAPP) in the blood of individuals with autism.

These findings suggest that amyloid beta peptides may play a role in the neurodevelopmental abnormalities seen in autism, although the exact mechanisms are still being studied.



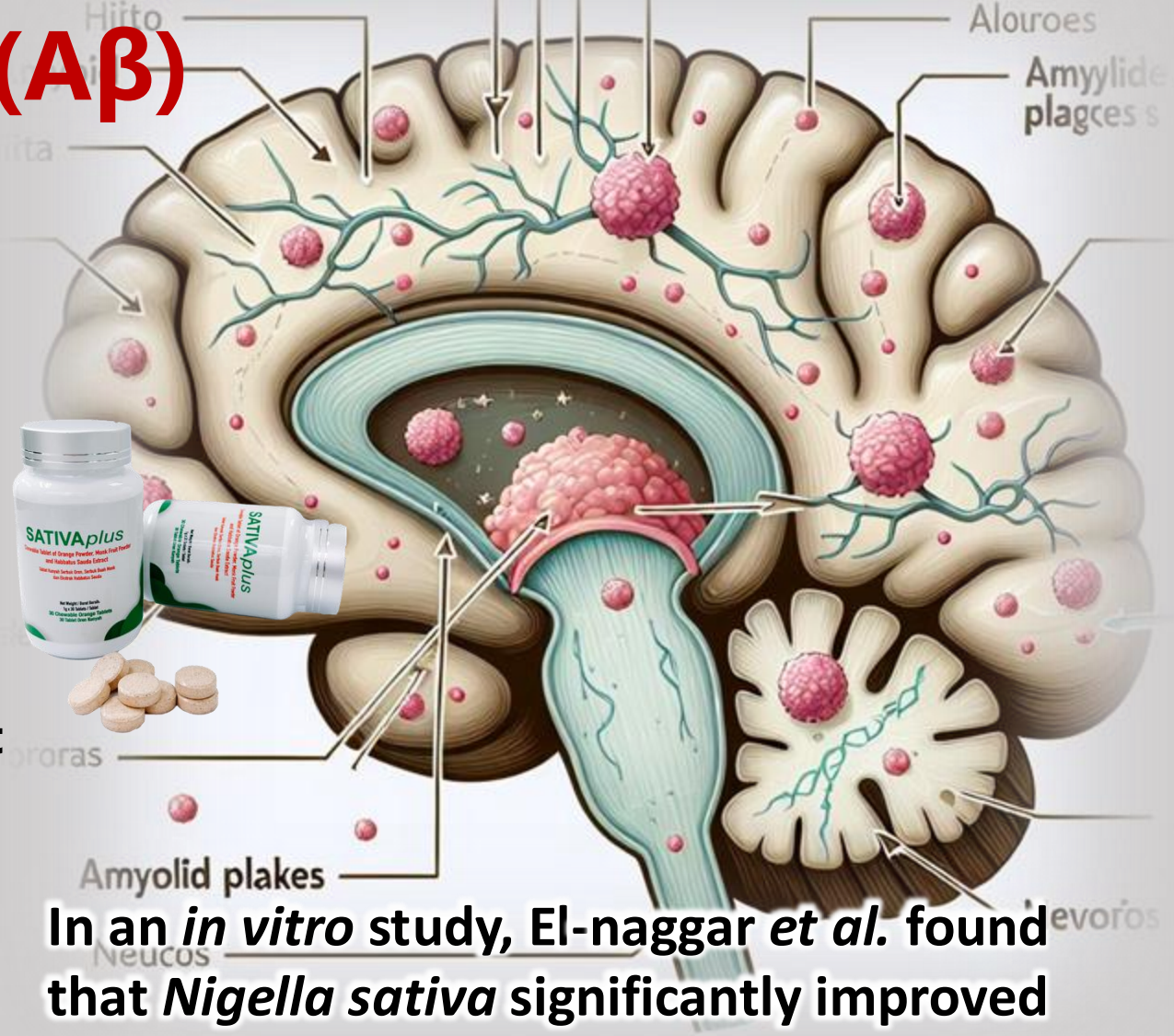
Amyloid beta peptide (Aβ)

ROLE OF NIGELLA SATIVA

Anti-Amyloid Aggregation: Thymoquinone, have been shown to inhibit the aggregation of amyloid beta peptides. This can help prevent the formation of amyloid plaques, which are characteristic of Alzheimer's disease.

Neuroprotective Effects: Black seed extracts have antioxidant properties that can protect neurons from oxidative stress, which is often associated with the accumulation of amyloid beta

Anti-Inflammatory Properties: The anti-inflammatory effects of black seed may also play a role in reducing the neuroinflammation that accompanies amyloid beta accumulation1



In an *in vitro* study, El-naggar *et al.* found that *Nigella sativa* significantly improved neuronal cell viability compared to untreated cerebellar neuron cell culture and protected against beta-amyloid protein intoxication (El-Naggar eta l., 2010).

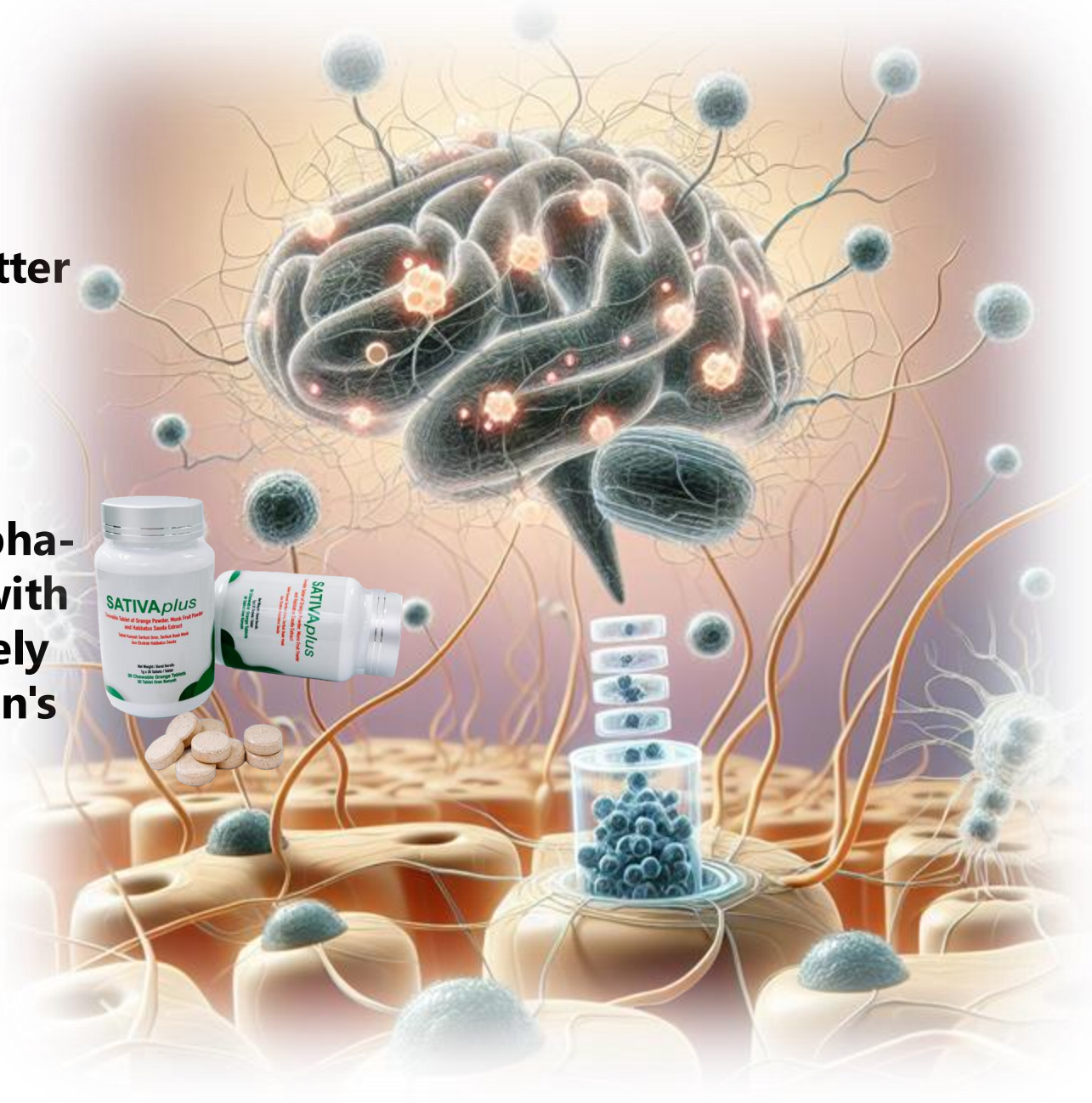
α-synuclein

α-synuclein is a protein primarily found particularly in the presynaptic terminals of neurons. It plays a crucial role in regulating synaptic vesicle trafficking and neurotransmitter release.

Function: It helps in the release of neurotransmitters.

Pathology: Misfolding and aggregation of alpha-synuclein into amyloid fibrils are associated with several neurodegenerative diseases, collectively known as synucleinopathies, such as Parkinson's disease2

•. In these conditions, alpha-synuclein accumulates in structures called Lewy bodies within neurons



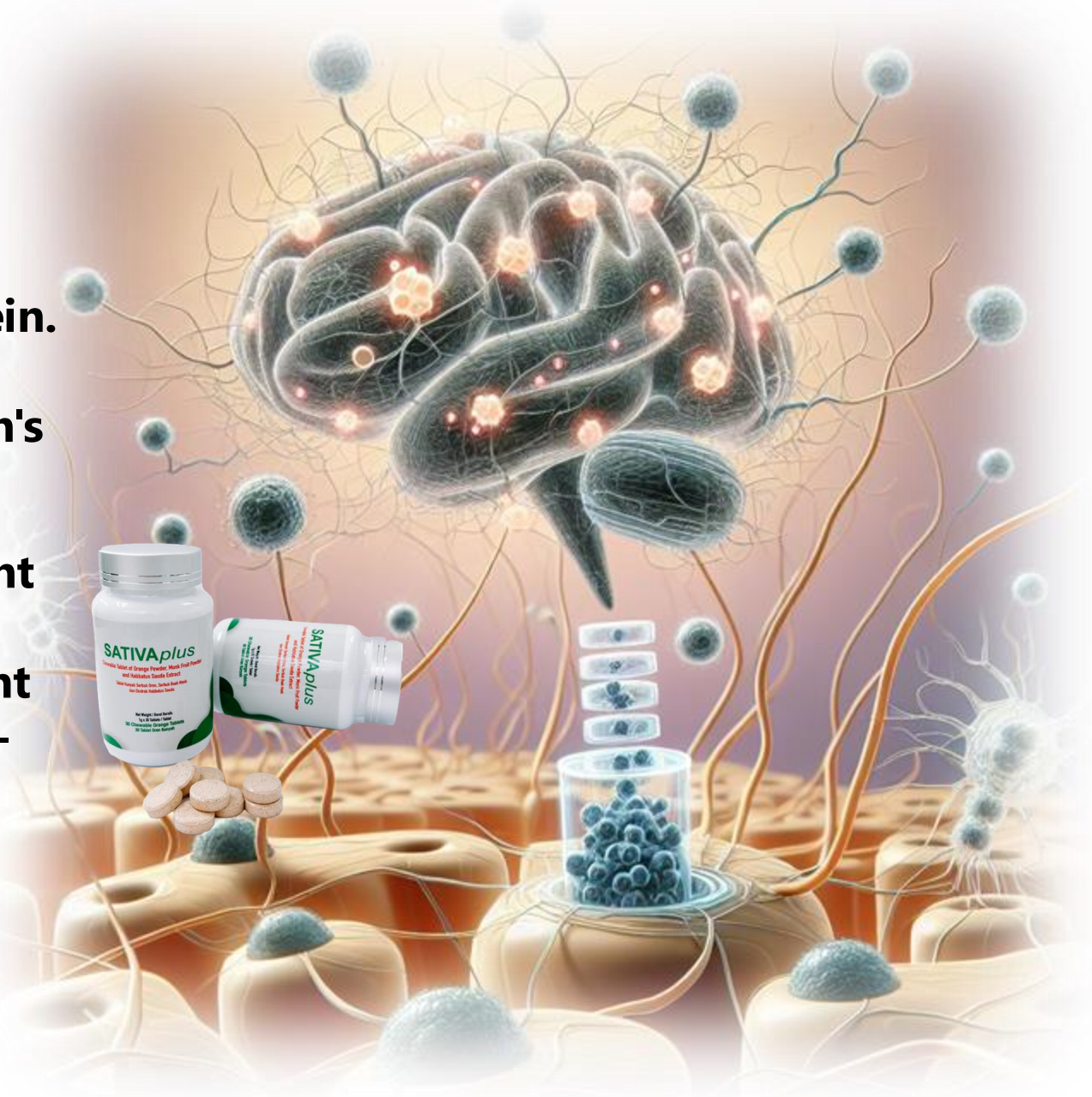
α-synuclein

ROLE OF NIGELLA SATIVA

Anti-Aggregation: Thymoquinone, have been shown to inhibit the aggregation of α-synuclein. This can help prevent the formation of toxic aggregates that are characteristic of Parkinson's disease

•Antioxidant: Black seed has strong antioxidant properties, which can protect neurons from oxidative stress. Oxidative stress is a significant factor in the misfolding and aggregation of α-synuclein

Anti-Inflammatory:: The anti-inflammatory properties of black seed may help reduce neuroinflammation.



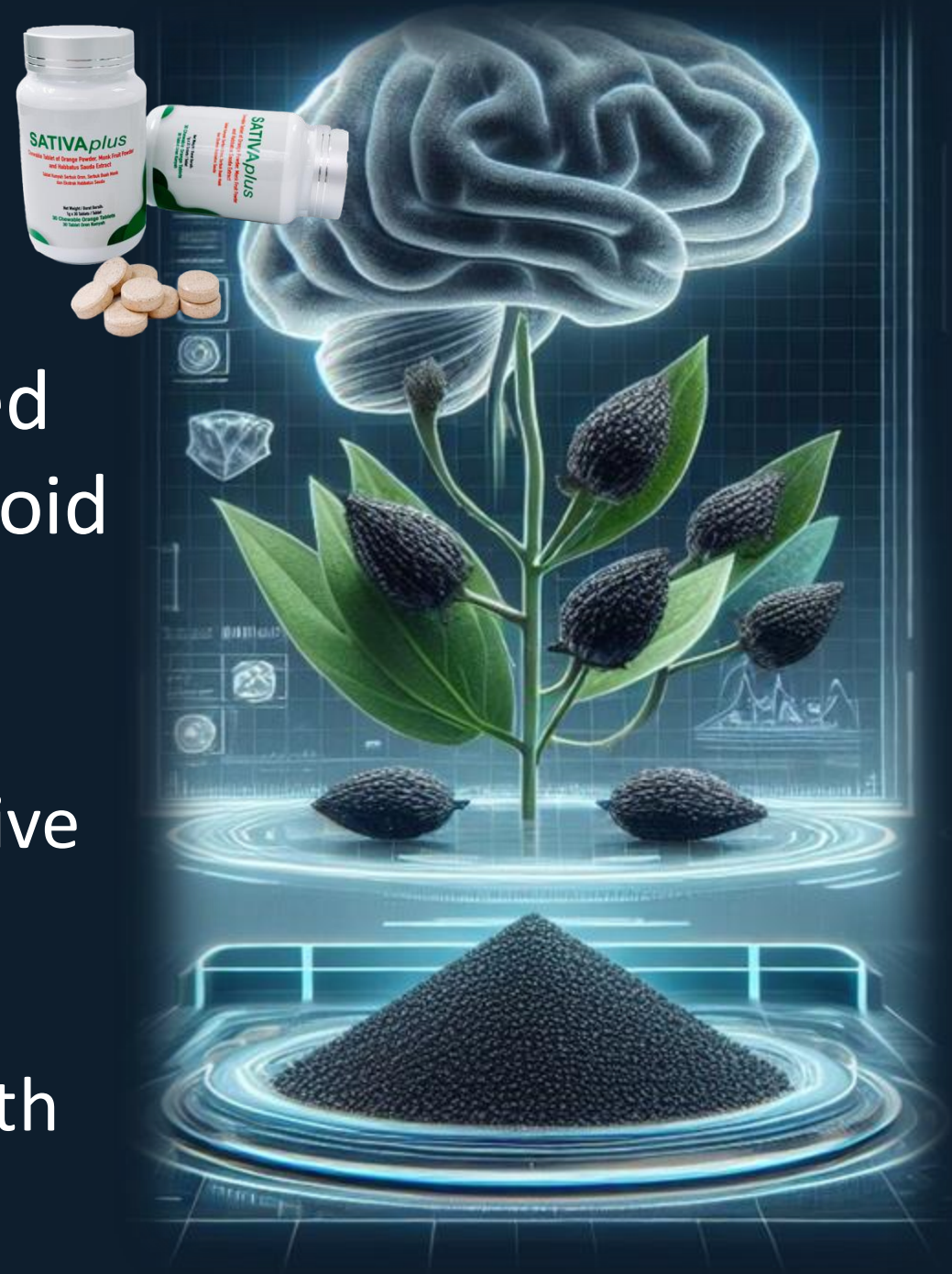

PROTECTION FROM
ALZHEIMER'S AND
PARKINSON'S
DISEASE

Alzheimer's disease is characterized by two abnormalities in the brain:
amyloid plaques and neurofibrillary tangles.

Amyloid plaques, found in the tissue between the nerve cells, are unusual clumps of a protein called **beta amyloid** along with degenerating bits of neurons and other cells.

The amyloid β peptide **(Aβ)** is **a critical initiator that triggers the progression of Alzheimer's Disease via accumulation and aggregation.**

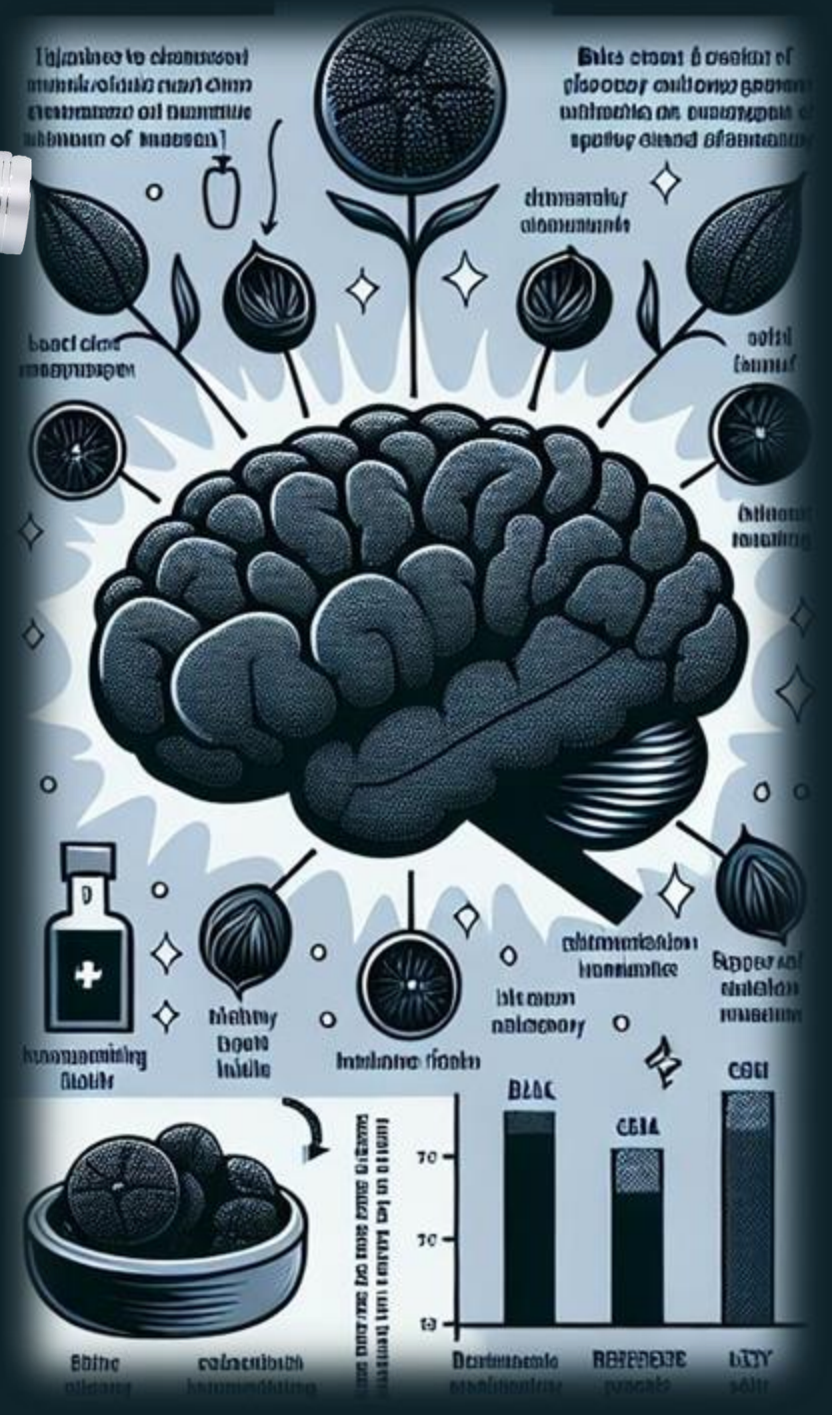
Thymoquinone protected cultured hippocampal and cortical neurons of embryos of Wistar rat brain against neurotoxicity and cytotoxicity induced by Alzheimer’s disease–specific amyloid beta (Alhebshi et al, 2013).



Alhebshi *et al*. also reported the protective effects of thymoquinone against the synaptic toxicity of α-synuclein, which is accumulated in the brains of patients with **Parkinson's disease and dementia.**

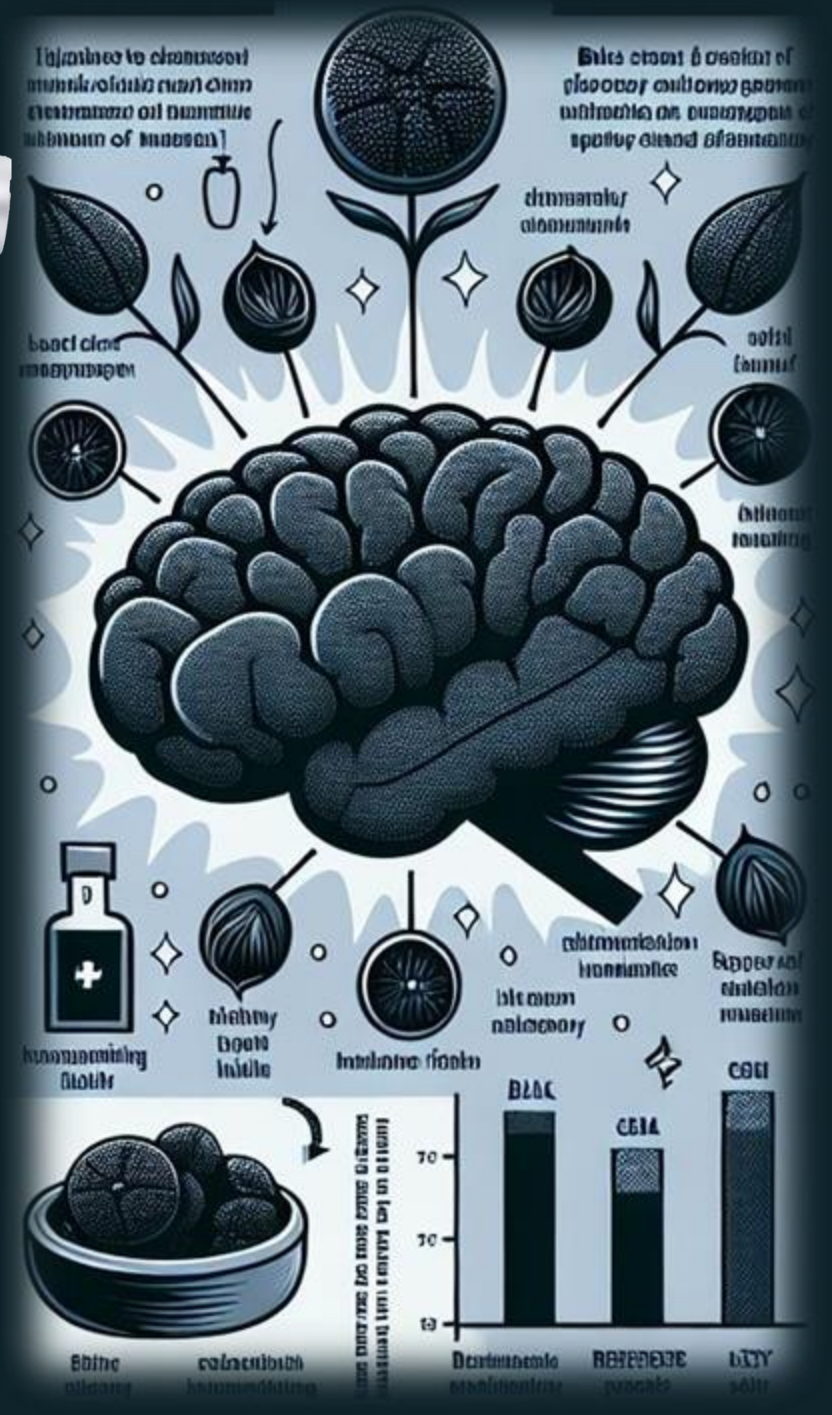
Nigella sativa in learning and memory impairments

- Many studies have been done to evaluate the effects of *Nigella sativa* on learning and memory.
- *Nigella sativa* can improve learning and memory.
- The proposed mechanism(s) for this effect are anti- inflammatory, antioxidant as well as anti-cholinesterase properties.



Nigella sativa in learning and memory impairments

Acetylcholine has an important role in the encoding of new memories (Hasselmo, 2006; Nabeshima, 1993). Enhancement of cognition and improvement of memory in groups treated with Nigella sativa might be due to activation of the cholinergic system in hippocampus that plays an important role in learning and memory.

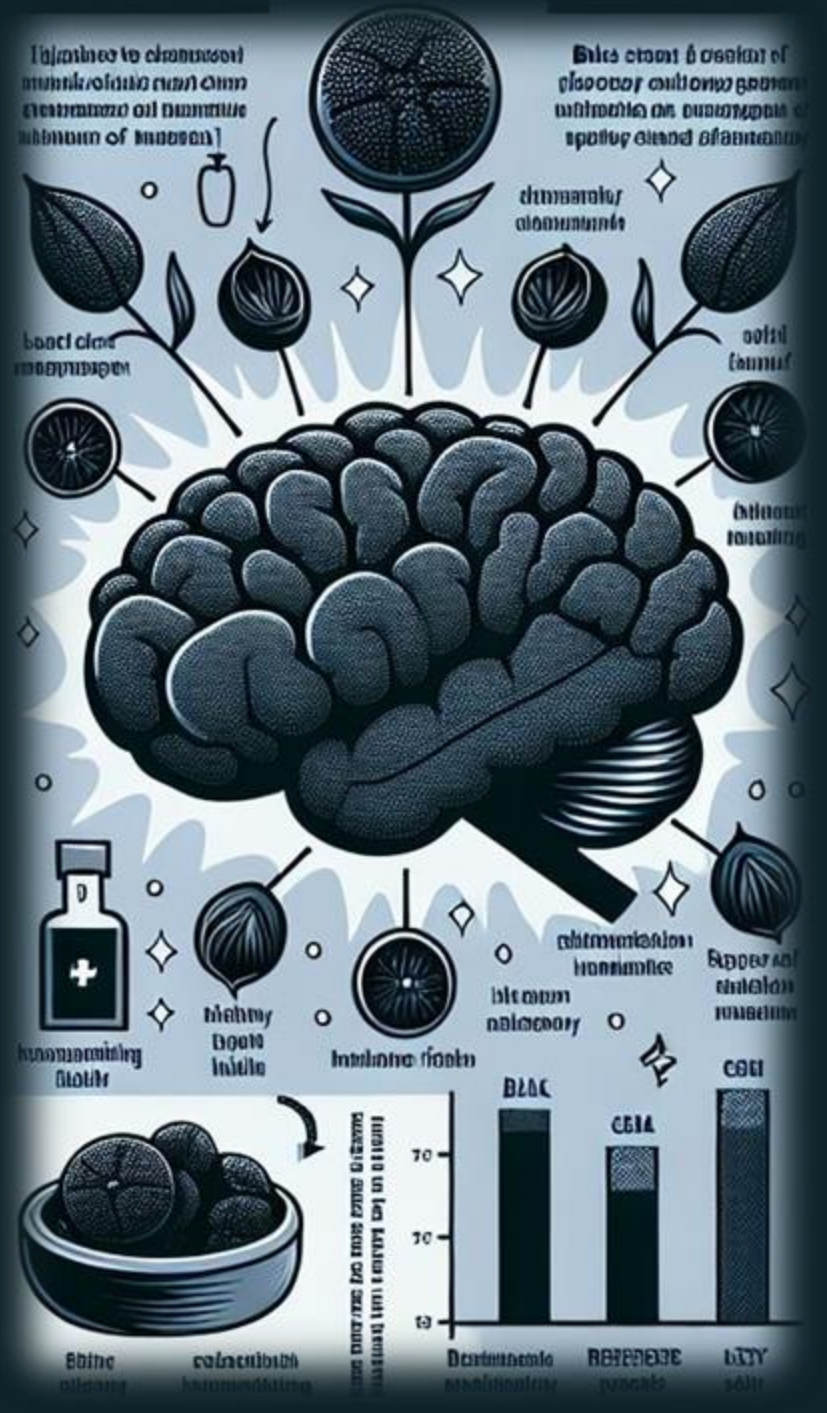


Nigella sativa in learning and memory impairments

A relationship between memory impairment and increased oxidative stress in the brain has been well documented.

Since oxidative stress is characterized by an imbalance in production of reactive oxygen species (ROS) and antioxidative defense, both are considered to have a noteworthy part during the time spent age-related neurodegeneration and cognitive decline

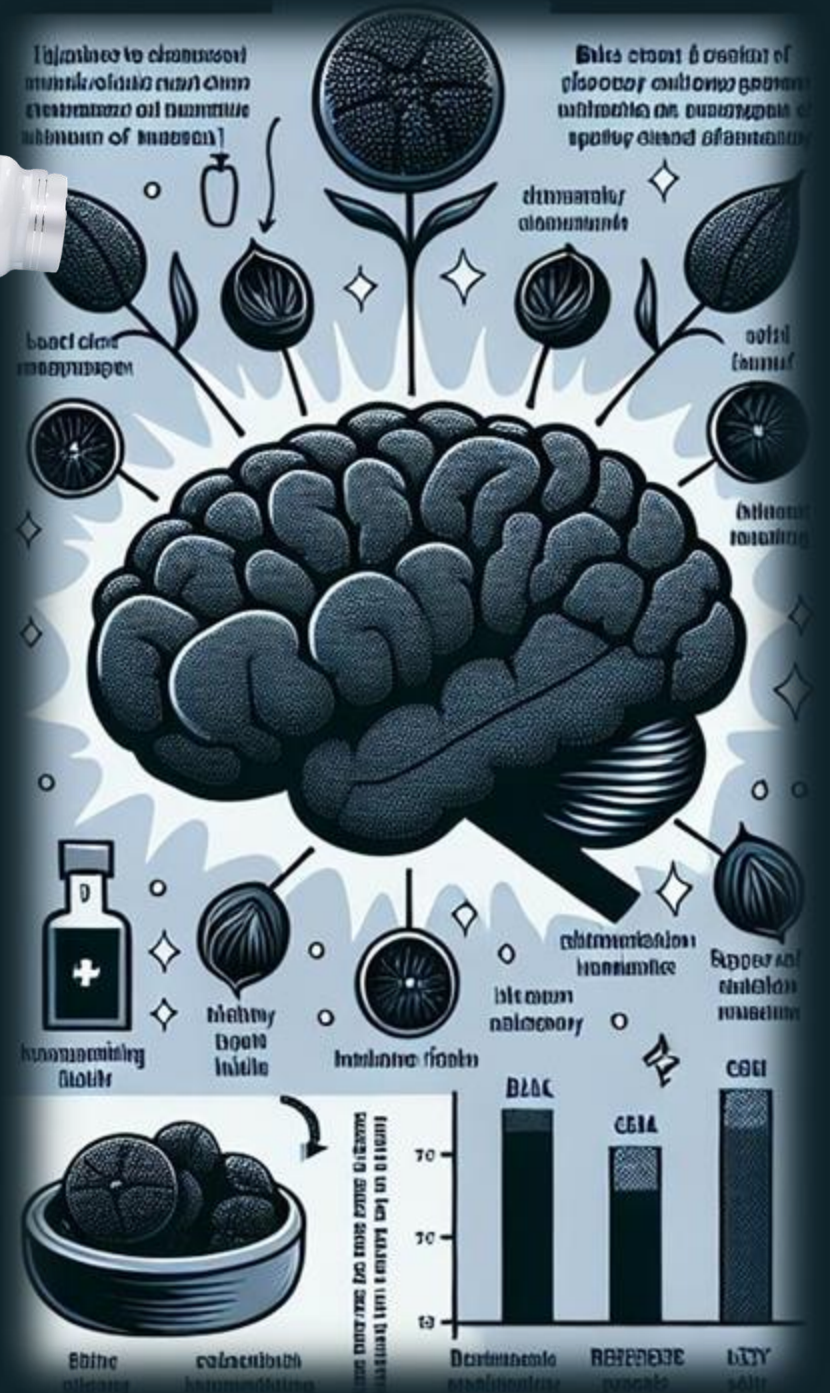
It has also been proposed that the improving effects on memory, cognition and attentiveness in NS-treated elderly individuals are due to anti-cholinesterase property of NS (Yassin, 2005).



Nigella sativa in learning and memory impairments

A previous study demonstrated that chronic oral administration of Nigella sativa oil could enhance the consolidation and recall capability of stored information and spatial memory in diabetic animals (Jalali and Roghani, 2009).

Administration of extract of Nigella sativa for two weeks could avert scopolamine-induced memory deficit in rats, as the animals showed better execution in passive avoidance tests and diminished acetylcholinestrase (AChE) activity in the hippocampus and cortex tissue of the brain (Hosseini et al., 2015).



Nigella sativa, anxiety and depression

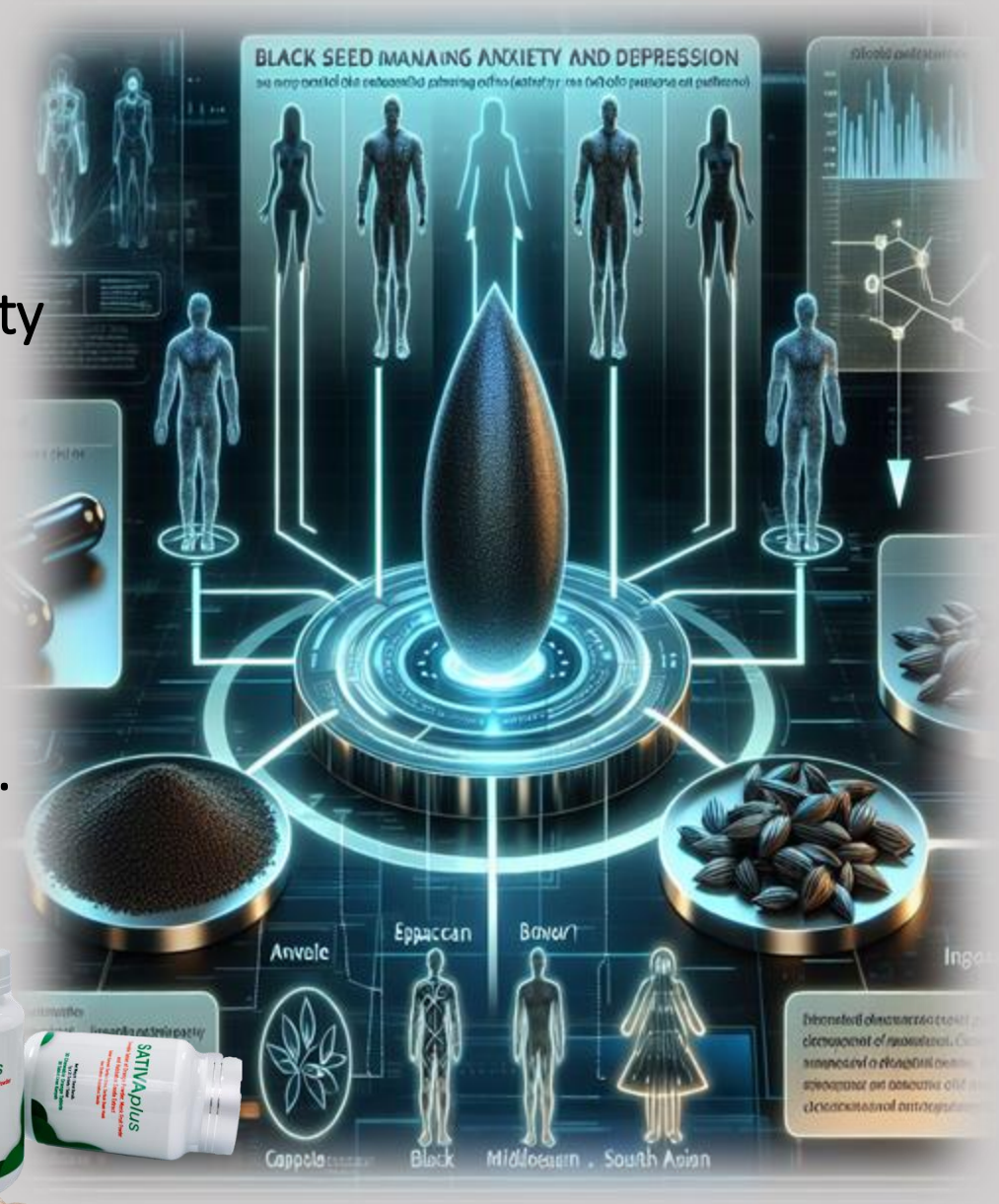
- Depression is the second most common chronic disease throughout the world.
- Estimated that about half of the patients are unaware of their disease or their disease is misdiagnosed
- Anxiety is also a complicated disorder in human and animals which may lead to a wide range of problems in the central nervous system (CNS).
- It has also been reported that anxiety affects one-eighth of the population and in severe forms it has debilitating effects on the quality of life

Nigella sativa, anxiety and depression

The open field test is an experiment used in scientific researches to assay general locomotor activity levels, anxiety and sometimes depression in rodents.

Forced swimming test is another test focusing on rat's reaction to the danger of suffocation and its results are translated as powerlessness due to negative mood.
It is usually used to gauge the adequacy of antidepressants.

Elevated plus maze is a well-known research tool in neurobiological anxiety research and is used as a scree test for putative anxiolytic or anxiogenic compounds



Nigella sativa, anxiety and depression

- Following daily administration of *Nigella sativa*l, showed an increment in open field activity.
- The animals had a better performance when tested in elevated plus maze.

- An oral administration of *Nigella sativa* raised brain levels of 5-hydroxytryptamine (5-HT), but the levels of brain hydroxyindole acetic acid (5-HIAA) significantly reduced (Perveen et al., 2009).

- Likewise, brain and plasma levels of tryptophan increased after repeated oral administration of Nigella sativa.

- Thymoqionone has also shown an anti-anxiety-like effect in mice through modulation of γ-aminobutyric acid (GABA) and nitric oxide (NO) levels in the brain or plasma.

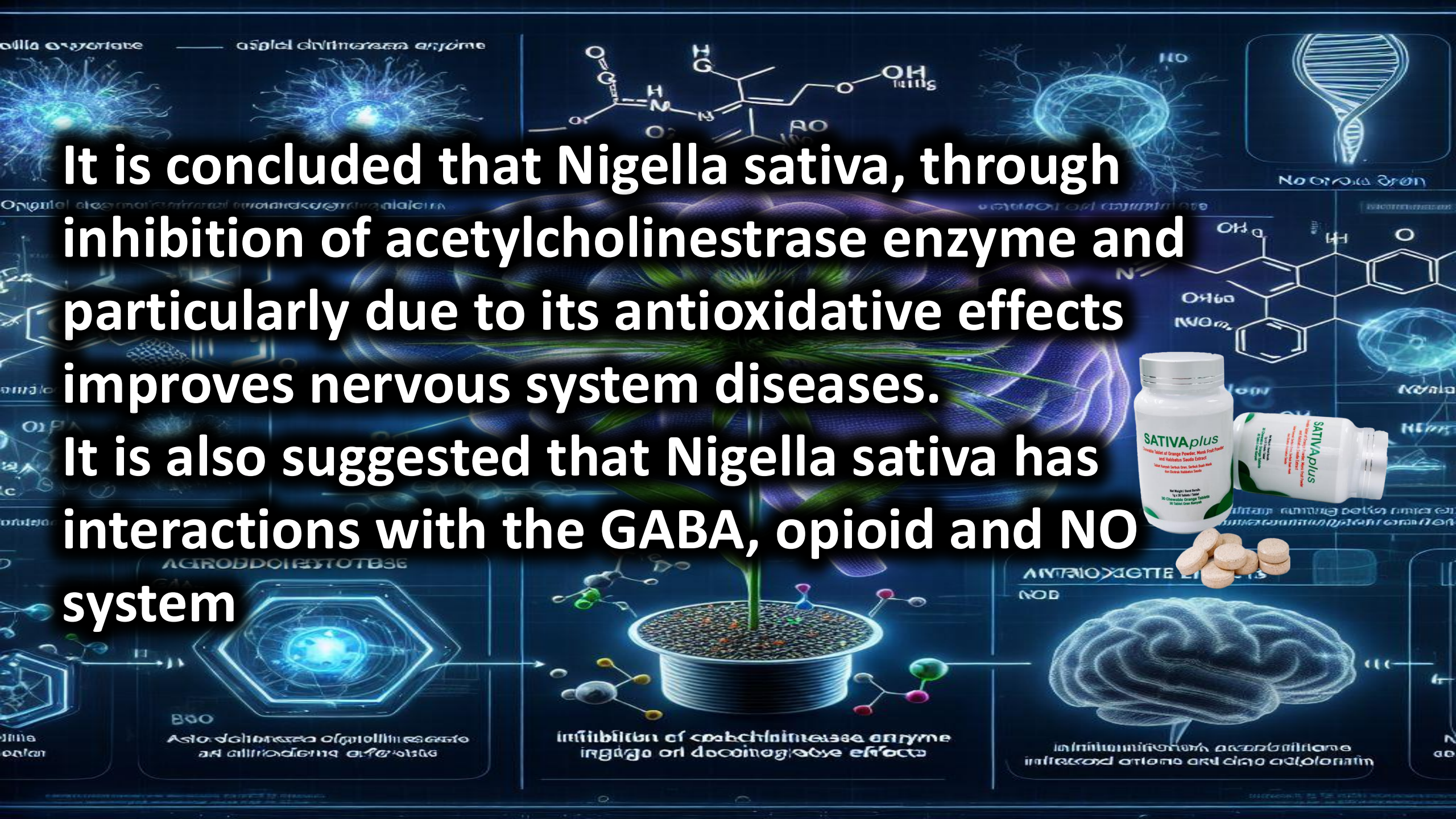
Nigella sativa, anxiety and depression

In another study, mice were subjected to 6 h immobilization in order to experience stressed conditions and the role of GABAergic and nitriergic modulation in the anti-anxiety effect of Thymoquinone has been investigated.

Thymoquinone produced significant anti-anxiety effects in unstressed mice without altering nitrite levels, but only the higher dose of thymoquinone increased the GABA content in unstressed mice.
In stressed mice, TQ showed anxiolytic effects with a significant reduction in plasma nitrite and brain GABA content.
Hence, an association between NO-cGMP and GABAergic pathways in the anxiolytic-like activity of TQ has been proposed (Gilhotra and Dhingra, 2011).

It is concluded that Nigella sativa, through inhibition of acetylcholinestrase enzyme and particularly due to its antioxidative effects improves nervous system diseases.

It is also suggested that Nigella sativa has interactions with the GABA, opioid and NO system



PENAWAR HERBAL MEDICINE SDN BHD
(1406616-H)

Presenting to you the ONE and ONLY ONE.....

SATIVA *plus*

"Healing power with herbs"

http://www.penawarherbalmedicine.com/

SATIVA*plus* *also contains Monk fruit.*

What is monk fruit?

Siraitia grosvenorii

Luo han gu

It is native to southern China

A small round fruit that is native to southern China.
It has been used for centuries in Eastern medicine as a cold remedy, sore throat, cough and digestive aid.

The plant is cultivated for its fruit extract, called mogrosides, which creates a sweetness sensation 250 times stronger than sucrose.

The BEST Black Seed /Habbatusauda product

A product for the PRESENT and the FUTURE

ONE tablet for ONE Million cure

ProfMUS

Exploring the therapeutic potential of *Nigella sativa* (Habbatusauda) in Autism spectrum disorder :

A comprehensive analysis of benefit and mechanism.

Thank You

Dr. Mustafa Ali Mohd. *FASc*
MALAYSIA