



## Therapeutic Potential Of Benincasa Hispida For The Treatment Of Alzheimer Disease

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Article History	Abstract
Received: 25-01-2024 Revised: 05-02-2024 Accepted: 14-02-2024	This article provides details on the annual climbing plant <i>Benincasa hispida</i> , a natural herb from the cucurbitaceae family.. The fruit is also called as winter gourd, ash gourd and kushmanda fruit. It is the most well-liked herb that is readily available to communities for medicinal and nutritional purposes. The phytochemical review indicates the presence of pentacyclic triterpene, flavonoids, volatile oils, bryonolic acid, alnusenol, multiflorenol, isomultiflorenol, lupeol, $\beta$ -sitosterol etc. <i>Benincasa hispida</i> fruit is one of incredible fruit which can improve health, treat a variety of illnesses and prevent many more. Pharmacological studies have revealed that the <i>Benincasa hispida</i> plant is useful in the treatment of several nerve diseases, including peptic ulcer, diabetic mellitus, internal organ hemorrhages, jaundice, epilepsy, and Alzheimer's disease.. The review mainly focuses on the effect of the fruit <i>Benincasa hispida's</i> potential to treat alzheimer's disease. This article covers all relevant information regarding <i>Benincasa hispida</i> with both historical and contemporary examples.
CC License CC-BY-NC-SA 4.0	<b>Keywords:</b> <i>Benincasa hispida</i> , Ash Gourd, Antioxidant, Beta Carotene, Alzheimers disease, Amyloid plagues

### INTRODUCTION:

On numerous occasions, people still use conventional medical systems. The focus on using plant materials as a source of medicines for a variety of human ailments has increased due to a growing number of factors such as population growth, a lack of medications, prohibitive costs of treatments, the side effects of many allopathic medications and the emergence of drug resistance to currently recommended medications for infectious diseases. *Benincasa hispida* is recommended in Ayurveda for treating peptic ulcers, internal organ hemorrhages, epilepsy, and other mental illnesses[1].

*Benincasa hispida* belongs to the cucurbitaceae family and is sometimes referred to as wax gourd, winter melon, white gourd, Chinese watermelon, ash gourd, tallow gourd, gourd melon. It was probably first cultivated in Java and Japan. They are now grown widely in India and other warm regions. It is a popular vegetable crop, especially in Asian communities, for its nutritional and medicinal qualities[2]. The plant develops thick, hairy stems and vines. It has broad, rough leaves that range in width from 4 to 12 inches (10 to 30 cm) long. Golden

yellow blooms start to appear in the leaf axils in early summer between June and September. they produce spherical, 50–60 cm long by 10–25 cm wide fruits after fertilization; the young fruits are covered in soft, fluffy hairs that gradually fall off and give way to a waxy covering that extends the fruit's shelf life to up to a year.

### Scientific Classification:

**Botanical Name:** *Benincasa Hispida*

**Table 1:** Scientific classification of *Benincasa hispida*[3]

<b>Kingdom</b>	Plantae
<b>Clade</b>	Angiosperms
<b>Order</b>	Cucurbitales
<b>Clade</b>	Eudicots
<b>Family</b>	Cucurbitaceae
<b>Genus</b>	Benincasa
<b>Species</b>	Hispida



**Fig 1.** *Benincasa hispida* Fruit

### Chemical Constituents:

The following chemical components are present throughout the entire *Benincasa hispida* plant[4]

**Table 2:** Chemical constituents of *Benincasa hispida*

Sr.No	Plant Part	Chemical Constituents
1	Root	Bryonolic acid, pentacyclic triterpene.
2	Fruit	Adenine, beta carotene, trigonelline, histidine, pentacyclic triterpenes, hexanal, and pyrazine chemicals as well as lupeol, -sitosterol, cucurbitin, rhamnose, mannitol, triacontenol, and alnusenol.
3	Seed	Multiflorenol, isomultiflorenol, 24-ethyl cholesterol and cholesterol-7-enol

Among the nutrients, it is high in vitamin C and carbohydrates. The following is a breakdown of *Benincasa hispida* nutritional value per 100 grams[5].

**Table 3:** Nutritional Values of *Benincasa hispida*

Nutrients	Percentage or per 100gm
Calories	13kcal
Macronutrients	3g
Carbohydrates	0.4g
Protein fat	0.2g
Micronutrients	13mg
Vit. C	0.11mg
Vit B2	0.4mg
Vit B3	0.133mg
Vit B	19mg
Calcium	111mg
Magnesium	0.11mg
Phosphorus	0.4mg

### Pharmacological Activities of *Benincasa hispida*[6,7]:

1. For the treatment of chronic inflammatory diseases, diuresis, urinary infections, and diabetic mellitus

2. For the treatment of epilepsy, peptic ulcers, Internal organ haemorrhages
3. For the treatment of histamine induced bronchospasm
4. Significant antiulcer, antidepressant & diuretic action were found in the juice and extract of *Benincasa hispida*

#### **Antioxidant activity:**

When compared to ascorbic acid, the methanolic extract of *Benincasa hispida* seeds demonstrated a substantial dose-dependent free radical scavenging efficacy[7]. At a concentration of 300 mg/ml, the extract exhibited the highest level of radical scavenging activity which was found to be 79.8%. The extract exhibited 63.7% H<sub>2</sub>O<sub>2</sub> scavenging efficacy when given dose of 200 mg/ml[8]. The study utilised traditional Soxhlet extraction (CSE) to investigate the effects of various solvents including n-hexane, ethanol and ethyl acetate on the total phenolic content (TPC) and antioxidant activity of the *Benincasa hispida* seed extract. Results from TPC, DPPH and ABTS scavenging activity tests showed that ethanol seed extracts had the highest antioxidant activity followed by n-hexane and ethyl acetate[9]. Methanolic and aqueous extract of *Benincasa hispida* showed significant neuroprotective potential by reducing the oxidative stress brought on by the injection of D-galactose. Catalase and glutathione peroxidase are activated in order to reduce lipid peroxide damage and have neuroprotective effects[10].

#### **Central Nervous Effects:**

On a mouse model of seizures brought on by pentylenetetrazole, strychnine, and the maximal electroshock test (MEST), the alcohol extract of *Benincasa hispida* was examined for its anticonvulsant effects. Animals were shielded from the most severe convulsions that electroshock might cause and had shorter mean convulsion recovery times thanks to the alcohol-based *Benincasa hispida* extract. Additionally, it prevented mice from developing convulsions caused by strychnine and shown anticonvulsant effectiveness against convulsions caused by pentylenetetrazole[11]. Swiss male albino mice were used to assess the methanolic extract's antidepressant effectiveness in comparison to traditional antidepressants such as phenelzine (20 mg/kg), imipramine (15 mg/kg) and fluoxetine (20 mg/kg). The extract was supplied orally for 14 consecutive days at doses of 50, 100 and 200 mg/kg. The methanolic extract of *Benincasa hispida* showed a significant antidepressant-like effect in mice which was probably brought on by inhibition of MAO-A and interactions with the dopaminergic, GABAergic, 1-adrenergic, and serotonergic systems[12]. The aqueous extract of *Benincasa hispida* pulp (400 mg/kg bw) was continuously administered as a treatment for the Alzheimer's disease-induced rat model. Additionally, it improved the number of accurate decisions made out of ten trials per day, boosted antioxidant levels in several brain regions, and reduced latency time dosage dependently[13].

#### **Diuretic Activity:**

In addition to the treatment modules, normal saline was given to induce diuretic and natriuretic action. Measurements were made of the urine's volume (in millilitres) as well as its Na<sup>+</sup>, K<sup>+</sup>, and Cl<sup>-</sup> contents. Not potassium, but a sizable diuresis and enhanced salt elimination are evident. According to the study, there is a significant amount of diuretic, saluretic, natriuretic, and carbonic anhydrase action in the *Benincasa hispida* stem extract prepared in ethanol[14].

#### **Anti-Inflammatory Activity:**

The study demonstrates the fruit of the *Benincasa hispida* has anti-inflammatory properties when extracted with petroleum ether and methanol. At a dose of 300 mg/kg body weight, both extracts effectively and dose-dependently reduced the rat model's paw edema caused by carrageenan, granuloma caused by cotton pellets, and paw edema caused by histamine. The anti-inflammatory qualities of fruit peel methanolic extract were well tolerated by rats subjected to egg albumin-induced inflammation[15].

#### **Cytotoxic Effects:**

Cancer is a genetic disease. It advances through a multi-step carcinogenesis process that involves many of the body's physiological systems. This involvement makes treating cancer very challenging. Cancer first manifests as a localized condition, but with time it may spread to other body areas, making therapy challenging[16]. The biosynthesised silver nanoparticles' half maximum inhibitory concentration (IC<sub>50</sub>) value against the human cervical cancer cell line was 0.066 g/mL; however, there was no cytotoxic effect observed on the normal human osteoblasts cell line[17].

#### **Anti-ulcer Effects:**

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Peptic ulcers are sores caused by acid that are frequently found in the duodenum and stomach. They are distinguished by a defect spreading into the submucosa or muscularis propria and a denuded mucosa[18]. In the model of diarrheal rats induced by castor oil, the methanolic fruit extract of *B. hispida* has shown encouraging antidiarrheal activity. Furthermore, in rats fed charcoal, it was found to decrease enter pooling, PGE2 production, and gastrointestinal motility[19].

#### Effect on Renal System:

The diuretic efficacy of extract from the fruit rind of *Benincasa hispida* (25–200 mg/kg) was tested in adult male guinea pigs. Urinary volume significantly increased as a result of the extract. The excretion of sodium and chloride increased significantly, while the excretion of potassium decreased[14].

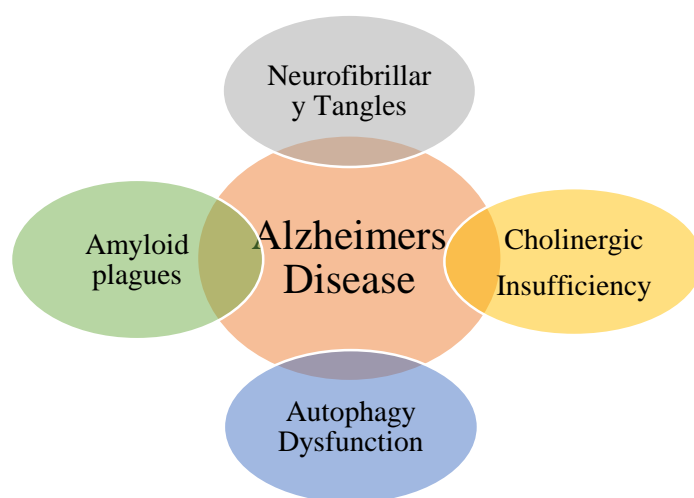
#### TOXICOLOGICAL PROFILE:

##### Safety and Adverse effects:

1. At concentrations of up to 3 gram per kilogram, the methanolic fruit extract was not lethal to mice, rats, or guinea pigs[20].
2. The fresh juice treatment (5% v/v) had no effect on the levels of sugar, urea, hematocrit, mean corpuscular volume, total RBCs, WBCs, haemoglobin, or mean corpuscular haemoglobin in rats or mice. Additionally, the therapy had no behavioural effects on the test animals[1].
3. Di-2-ethylhexyl phthalate (18.3-75.5 mg/kg), a common plasticizer derived from this herb's fruit is harmful to human health[21].
4. The extract displayed no noticeable side effects in the 90-day toxicity testing up to oral dose level (1000 mg/kg/day). Rats given up to 5000 mg/kg of the ethanolic seed extract were not intoxicated[22].

#### BENINCASA HISPIDA IN THE TREATMENT OF ALZHEIMERS DISEASE:

Alzheimer's disease (AD) is a degenerative brain disease that mostly affects older adults. It is characterised by a gradual loss of cognitive abilities[23]. Alzheimer's disease is one of the most common causes of dementia that affects nerve cells across the brain is Alzheimer's disease. This neurodegenerative disease is caused by extracellular amyloid protein and intracellular neurofibrillary tangles, which lead to the formation of plaques that interfere with nerve cell transmission. Though the precise cause of the disease is still unknown, researchers have found that individuals with Alzheimer's have an unusual buildup of specific proteins in their brains. 'Plaques' are formed when amyloid beta, one of these proteins, gathers. Researchers continue to investigating whether these alterations in the brain underlie the symptoms of AD.



**Fig 2.** Pathophysiology of Alzheimers Disease

#### Applications of *Benincasa hispida* in the treatment of Alzheimers disease:

**Table 4:** Anti-alzheimer's activity of *Benincasa hispida*

Sr No.	Benincasa hispida dosage for Alzheimer's disease	Test	Results
1	250 mg/kg/day and 500 mg/kg/day for 16-weeks	Y-maze, rotarod, and Morris test water maze	The levels of the neurotransmitters acetylcholine, dopamine, and serotonin were reduced. The oxidative stress marker malondialdehyde was lowered, but the enzyme indicators of catalase, glutathione and superoxide dismutase were elevated[24].
2	250 mg per kg and 500 mg per kg orally and once every seven days	Stress induction	In terms of reducing stress induction, the 500 mg per kg dose of <i>Benincasa hispida</i> and MDA were statistically significant (p-value 0.05 and >0.05, respectively). Despite the lack of a substantial change in antioxidant levels. This study showed that <i>Benincasa hispida</i> has a positive impact on a whole animal model of stress[25].
3	400 mg/kg body wt.	Radial Y Arm Study (Holtzman Strain adult albino rat)	Results indicated that, chronic treatment of <i>Benincasa hispida</i> at different doses can increase the CAT, SOD, GSH levels along with reduced latency time and dose-dependent lipid peroxide oxidase level[26].
4	400 mg/kg body wt.	The significance level between the means was determined using the Student t test.	On days 7, 14, and 21, <i>Benincasa hispida</i> significantly increased catalase, glutathione and superoxide dismutase activities while decreasing lipid peroxide oxidase level and After a certain amount of co-administration, the aqueous pulp extract of <i>Benincasa hispida</i> (400 mg/kg body weight) containing vitamins C, E, and A significantly protects the level of antioxidant status in the frontal cortex and hippocampus[27].

## CONCLUSION:

The current study reviewed the most recent in vivo and in vitro pharmacological investigations that illustrated the molecular processes supporting the ethnopharmacological uses starting with these traditional applications. The *Benincasa hispida* has wide applications in the treatment of various diseases such as chronic inflammatory diseases, diuresis, urinary infections, bronchospasm and diabetic mellitus etc. Methanolic and aqueous extract of *Benincasa hispida* demonstrated strong neuroprotective potential by lowering oxidative stress which is beneficial in the treatment of Parkinson's and Alzheimer's diseases in the future.

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