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Review Article

Ash Gourd in Modern Drug Delivery: Exploring Novel Formulations and its Applications

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ABSTRACT

The vegetable known as ash gourd [*Benincasa hispida* (Thunb.)] is used in numerous nations. Customers are searching for foods that are both nutritionally and functionally active. Typically the whole plant of the ash gourd is used including the seed, flower, fruit peel, and leaves. The biochemical activity of Ash gourd includes. anti-inflammatory, anti-angiogenic, detoxifying, oxidative, and curative effects in the treatment of different illness. It also contains Ca, Mg, Fe, Cu, Zn, and Se. The evaluation investigates the culinary and therapeutic applications of ash gourd.[1]

INTRODUCTION

Ash gourd, often known as wax gourd or hairy melon. In Ayurveda, winter melon, ash pumpkin, and "Kushmanda" are also important sources of nutrients. It is the sole species in the genus *Benincasa* used as a medicine [2,3].

Ash gourd grows in the wilds of South-East Asian nations like China, Nepal, India, Sri Lanka, and Indonesia, as well as in Australia's warmer southern areas. It is a creeper which gives big yellow flowers. The leaves of ash gourd are long, up to 10–20 centimeters, and the stem is hairy and long. The fruits can reach a diameter of up to 30 centimeters. The propagation of plants is carried

out with the help of seeds. When this vegetable is young, its thick, white flesh is sweet. By the time it reaches maturity, its hairs fall out and a waxy layer forms, giving it a long shelf life. Ash gourd juice and roots can also be used to treat skin and hair.

Moreover, (*Benincasa hispida*), ash gourd, commonly known as 'Kushmanda', has been used as a vegetable in various countries and has substantial therapeutic benefits. It has been utilized in Indian traditional medicine to treat a variety of conditions like diabetes mellitus, disorders of diuresis, urinary tract infections, and chronic inflammatory diseases, liver problems, heart problems, fever, cough, and epilepsy. It has

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solitary yellow flowers that are unisexual and 8–10 cm wide. Heart-shaped hairy leaves are found at the base and usually lobed in a palmate fashion. Fruit that is round or oblong can grow up to 40 cm in length and is frequently coated in a white, chalky substance that helps to impart durability to the gourd. The green, mature fruit has flat, white seeds that are about 1 cm long. The flavor is bland. A soil pH of 6.0 to 7.5 and warm, humid conditions with an ideal temperature of 24 to 30 °C are necessary for the development of ash gourd. The fruit takes on a variety of sizes, colors, and shapes [4].

The mean weight of fruit is between 0.5 and 3 kg, measures 18 to 35 cm in length, 15 to 33 cm in width, and 30 to 37 cm in circumference. The flesh

is greenish white, juicy, slightly fragrant, and spongy in the center, with a white, easily removable wax layer with lots of seeds. Oval, elliptical, flattened seeds that are 1–1.5 cm long and occasionally yellow-brown are characteristically ridged. Typically, harvesting begins 90–100 days after seeding and is finished in roughly 140–160 days. When the ashy or waxy bloom appears on the surface, the mature fruit is ready to be harvested [4]. The method of information gathering was identifying potential areas and research gaps for upcoming research using a medical and nutritional viewpoint. Being aware of the nutritional scientific research on the ash gourd's potential for medicine may impact the workspaces and customers in the appropriate guidance [2].



Fig1.Ash gourd

Phytochemistry of Ash gourd:

The bioaccessibility of ash gourd is influenced by phenolic and flavonoid compounds. Many phenolic substances found in plant-based foods have a wide range of chemical characteristics and structural formations, and aqueous mixes can be used to extract, isolate, and identify ethyl acetate, acetone, ethanol, and methanol. Ash gourd is rich in fats and dietary fiber, which results in a relationship between dietary polyphenols, sugar, and fiber, increasing their bioavailability. Ash gourd dietary fibers exhibit superior prebiotic activity. The bioactive, therapeutic, and

functionally significant compounds of ash gourd are phenolics, sterols, and glycosides, which can be used to treat ulcers, epilepsy, and other neurological conditions. The ash gourd has antacid properties which help to maintain the body pH and reduce the acidity caused by some foods. Ash gourd contains cucurbitacin B, which has cytotoxic and anti-inflammatory properties. Ash gourd contains active triterpenes; multiflorenol and alnusenol are inhibitors of histamine release. There are some anti-nutrients—oxalates, tannins, and phytates—present in ash gourd which are of concern because they have a detrimental impact on the availability of minerals. An increased amount

of oxalate in the diet increases the risk of calcium accumulation and has been identified as a source of kidney stones.



Fig.2 Phytochemistry of ash gourd.

Table 1:Physicochemical composition of pulp, peel and total fruit of ash gourd.[1]

Fruit part	Moisture (%)	Protein (g)	Fat (g)	Carbohydrates (g)	Zinc (mg)	Iron (mg)	Calcium (mg)	Fiber (mg)
Pulp	92.6	0.60	0.2	2.4	0.15	0.5	18	0.7
Peel	3.72	3.7±0.09	-	-	0.17	0.02	-	1.2
Total Fruit	96.21	13	-	3.95	0.7	11.9	31	2.8

Pharmacological activities of ash gourd

Juices from fruits and vegetables are essential to human diets due to their pleasant, satisfying, aesthetic, refreshing, and therapeutic properties. Ash gourd has a mild flavour and pale colour. It has outstanding values, offering significant and potentially life-saving health benefits. Despite its many health advantages, ash gourd is not used by a large population. Vegetable and fruit juices are crucial to human diets [5]. According to pharmacological research, *B. hispida* comprises crucial functions in the central nervous system as an antidepressant, muscle relaxant, and anxiolytic, for lowering opiate levels and in Alzheimer's disease, with antioxidant, anti-inflammatory, anti-nephroprotective, diuretic, asthmatic, antimicrobial, hypolipidemic, and antidiabetic properties [6]. Traditionally, the fruit is used as an

antibiotic and purgative, and for cough, fever, heart diseases, and liver disorders [7].

1. Improvement of digestion

Digestion is a complicated multiple-scale physiological procedure in the gastrointestinal system of humans that includes regulating food consumption and catabolism to the proper forms, assimilation of the fundamental units, conveyance to related tissues, and elimination of any leftover waste [8]. Food components and structure have an impact on nutritional and practical outcomes throughout the process of digestion [9]. Ash gourd is low in calories and rich in water, which may help promote digestion and improve healthy body weight. The presence of high soluble fiber content slows down digestion and promotes a feeling of fullness [10].

2. Prevention of ulcers

Acid reflux is a symptom of peptic ulcers. Induced lesions are frequently observed both in the duodenum and stomach. They are defined by a denuded mucosa with an extending defect into the muscularis propria or submucosa [11]. Ash gourd's medicinal properties include the ability to raise the gastric juice's basal volume and reduce the gastric juice's pH level by raising free gastric juice acidity and chloride secretion [12].

3. Anti-inflammatory activity

An immune system in good working order is essential for acute inflammatory response activation, which is required when there are severe wounds and infections. These acute reactions are important factors in attracting leucocytes as well as additional immune mediators to the locations of wounds and infections [13]. When chronic inflammatory stimuli occur, the person enters a state of persistent inflammation. Prolonged inflammation is responsible for raising the risk of a number of chronic illnesses such as diabetes, cancer, cardiovascular diseases (CVDs), and high blood pressure [14]. Ash gourd is among the most resilient food factors that influence long-term systemic inflammation [15].

4. Anti-bacterial and anti-microbial effects

Ash gourd has defense properties against some fungi and bacteria. Ash gourd seeds and pulp have demonstrated antimicrobial effectiveness against specific bacteria, both Gram-positive and Gram-negative [16]. A study conducted by Wadikar et al. showed that aqueous pulp extracts and seeds possessed antimicrobial properties, particularly with improved ability to combat *A. actinomycetemcomitans*, *Porphyromonas gingivalis*, *Prevotella intermedia*, and *Fusobacterium nucleatum* in contrast to other microbes.

Fruit ingredients that have antibacterial properties include triterpenoids, flavonoids, vitamins, sitosterin, carotenes, glycosides, saccharides, and uronic acid [17,18]. Hispidalin, a bioactive peptide in *B. hispida*, has significant medical importance, including antimicrobial activity. These active peptides act against harmful bacteria and fungi that affect humans and plants [19].

5. Antioxidant activity

Several epidemiological studies have revealed that consumption of dietary antioxidants is effective for positive health outcomes, decreasing risks of dangerous diseases as well as premature aging. In addition to proteins, fats, carbohydrates, vitamins, and trace elements, natural antioxidants are recognized as important components in healthy diets [20,21]. Spices, berries, chocolates, nuts, fruits, and vegetables all contain most of the antioxidants. Ash gourd is abundant in vitamin C and is an excellent source of carotenes and flavonoids, which serve as the body's antioxidants and offer protective impacts [21].

6. Diuretic activity

Diuretics are very helpful in the treatment of elevated blood pressure and mild to moderate hypertension, alongside additional antihypertensive medications. Furthermore, they alleviate peripheral and pulmonary congestion (edema) [22]. The diuretic properties of whole ash gourd have been revealed in traditional medicine, where ash gourd juice is used to lower blood pressure and kidney calculi. Researchers have found that ash gourd rind extract greatly raises sodium and urine volume, and excretion of chloride, while excretion of potassium declines [23].

7. Renal protective activity



Oxidative stress is caused by renal ischemia or reperfusion (I/R). The cause of impaired kidney function is stress, which results in notable elevations in serum levels of urea, creatinine, and uric acid [24]. Ash gourd is able to prevent renal I/R-induced lipid peroxidation and protects kidneys from severe attenuation. A study on animal models has shown that the antioxidant activity of ash gourd significantly improves impaired kidney function and preserves the morphological and cytological integrity of the kidneys [25].

8. Alzheimer's disease

Alzheimer's disease is most widely seen in elderly people. It was discovered by Alois Alzheimer in 1906. The symptoms of Alzheimer's disease include increasing memory loss, confusion, and related cognitive decline [26]. It is a neurodegenerative illness characterized by protein aggregation, oxidative stress, and inflammation [27]. According to an experimental study, fruit extract at a dose of 400 mg/kg effectively decreased colchicine-induced Alzheimer's disease in rats. This effect is attributed to the presence of vitamin E and β -carotene, which help protect against oxidative stress [28].

9. Anticancer activity

Ash gourd's antioxidant and apoptotic regulatory systems have demonstrated anti-cancer properties. Its bioactive components, flavonoids and triterpenoids, have been shown to have lethal impacts on cancer cell lines, specifically those of breast and hepatocellular cancer. Additional in vivo and clinical studies are required to confirm these results and evaluate the underlying molecular pathways, even though in vitro research has demonstrated promising anticancer potential. The main anticancer qualities of ash gourd are

derived from its antioxidant activity and regulation of apoptotic pathways. More investigation is necessary to clarify its precise strategies to combat different kinds of cancer cells [29].

10. Effects of anxiolytics and antidepressants

The potent anxiolytic and antidepressant properties of ash gourd are probably caused by changes to neurotransmitter pathways, such as dopamine and serotonin. According to a study in animal models, the anxiolytic effects of essential oil extracts were similar to those of well-known anxiolytic medications. Furthermore, another study revealed that extracts rich in alkaloids showed antidepressant effects in rats, indicating that ash gourd might be used to treat mood and anxiety disorders. More research is needed to clarify human molecular mechanisms, dose-dependent impacts, and confirm findings in animal models. The anxiolytic and antidepressant effects of ash gourd are most likely due to changes in neurotransmitter activity [29].

11. Antidiabetic activity

Ash gourd has been shown in numerous studies to have antidiabetic properties. Ethanolic extracts of ash gourd dramatically lowered blood glucose levels and enhanced lipid profiles in a rat model. Further studies have confirmed its hypoglycemic and hypolipidemic effects, indicating the possibility of using it as a natural treatment for diabetes [29].

12. Lipid-Lowering Effects and Anti-Obesity

Ash gourd's effects on adipogenesis and lipid metabolism have led to studies on its potential to reduce cholesterol levels. In a study with diet-induced obese mice, lyophilized ash gourd juice dramatically decreased serum triglyceride and LDL cholesterol levels while increasing HDL



cholesterol levels. Furthermore, the fruit's high dietary fiber content may help with weight management. Ash gourd has been shown to lower obesity rates as well as metabolic syndrome. Research has demonstrated that lyophilized ash gourd juice successfully reduces body fat [29].

13. Neuroprotective Activity

A dose-dependent anticonvulsant effect was demonstrated by the fruit methanol extract in strychnine, picrotoxin, pentylenetetrazole, and maximal electro-seizure models. Methanolic extract inhibited convulsions caused by pentylenetetrazole in a dose-dependent manner in mice. The anticonvulsant properties of ethanolic seed extract also showed dose-dependent impacts on Swiss albino mice, confirming its neuroprotective activity [27].

1. Ash gourd helps improve digestion.
2. Ash gourd is good for your lungs.
3. Ash gourd increases vitality.
4. Ash gourd is a natural ulcer remedy.
5. The ash gourd has anticoagulant qualities.
6. Ash gourd has cooling properties.
7. Ash gourd helps people relax.
8. Ash gourd controls the digestive system.
9. Dandruff is treated by ash gourd.
10. Ash gourd has the ability to moisturize.
11. Ash gourd has hydrating qualities.

Ash gourd benefits for better life [30]:

Table 2: Therapeutic activities of ash gourd.[29]

Sr No.	Activity	Description
1	Antidiabetic	Decreased blood levels of glucose in rats with diabetes using extract made with ethanol.
2	Anti-obesity	Juice that has been lyophilized relieves prediabetes symptoms as well as lowers body fat.
3	Anticancer	Cytotoxic consequences against cancerous cell lines, especially hepatocellular carcinoma.
4	Antidepressant	Anxiolytic as well as antidepressant impacts mediated by neurotransmitter modulation.
5	Antimicrobial	Prevention of both fungi and bacterial strains through phenolic substances.
6	Lipid-Lowering	Decrease in triglycerides and LDL, with a rise in HDL.

Side effects of ash gourd:

The following are some adverse effects of ash gourd juice:

Phytates, oxalates, and other anti-nutritional components found in ash gourd may lower the capacity of the body to absorb nutrients. A high diet in ash gourd could put you at risk for calcium

buildup, potentially resulting in calcium renal calculi. Numerous toxicological investigations indicate that ash gourd may be safe for animals and may not cause any negative side effects unless taken in excess [2].

Modern Drug Delivery Systems for Ash Gourd

1. Nanoemulsions



Water-in-oil or oil-in-water nanoemulsions enhance the oral absorption and solubility of lipophilic phytochemicals. They can be optimized for stability, zeta potential, and droplet size (less than 200 nm), and they are comparatively easy to prepare (high-shear, ultrasonication). Nanoemulsions have the potential to improve intestinal absorption and dissolution of ash gourd extracts that contain lipophilic flavonoids or terpenoids. Processing energy, surfactant/co-surfactant ratios, and oil type (MCT, long-chain triglycerides) are examples of formulation variables [31].

2. Polymeric Nanoparticles

Mucoadhesion and controlled release are made possible by biodegradable polymers (PCL, chitosan, alginate, and PLGA). Polymeric nanoparticle encapsulation can increase stability in the stomach, promote lymphatic absorption, and produce long-lasting plasma concentrations. Polymeric nanoparticles for ash gourd extracts can be engineered to release phytochemicals that are either antidiabetic or antioxidant at specific locations [32].

3. Liposomes and Phytosomes

By encasing hydrophilic and hydrophobic actives in bilayer vesicles, liposomes enhance absorption and shield labile substances. When compared to uncomplexed extracts, phytosomes (phospholipid-polyphenol complexes) frequently exhibit superior oral bioavailability and stronger interactions with plant polyphenols. Phytosome formulations are a promising method for *B. hispida* polyphenolic fractions and have shown success with silymarin and other plant polyphenols [33].

4. Metallic Nanoparticles

Extract phytochemicals from *B. hispida* have been utilized in a number of studies to biosynthesize metallic nanoparticles (AgNPs, AuNPs) by using them as capping and reducing agents. In early research, these "green" nanoparticles demonstrated antimicrobial and anticancer properties. Metallic nanoparticles (NPs) are promising, but they also present toxicity issues that require careful investigation, including in vitro cytotoxicity, hemocompatibility, and in vivo biodistribution/toxicity [34].

5. Hybrid and Targeted Systems

Combining strategies, such as ligand-targeted liposomes, stimuli-responsive carriers, or polymeric nanoparticles loaded with phytosomes, may result in synergistic enhancements in site specificity and delivery. Biomimetic coatings (cell-membrane camouflaging) and emerging smart nanocarriers may be studied for the targeted delivery of *B. hispida* phytochemicals to tumor or inflammatory tissues [31].

Formulation & Characterization Considerations

Important formulation endpoints for nanoformulations of *B. hispida*:

1. **Phytochemical standardization** – To guarantee batch consistency, measure marker compounds (such as specific flavonoids and polyphenols) using HPLC/LC-MS [35].
2. **Particle size & PDI** – Size and dispersity using dynamic light scattering; for stable systems, the PDI should be less than 0.3 and the target size should be less than 200 nm [32].
3. **Surface charge** – Affects mucoadhesion and stability.

4. **Encapsulation efficiency & release kinetics** – Determined using HPLC, a validated assay.
5. **Stability** – Assess stability under ICH conditions both chemically (marker compound degradation) and physically (phase separation).
6. **In vitro ADME/Tox** – Hemolysis, cytotoxicity (MTT), intestinal permeation models (Caco-2), and dissolution.
7. **In vivo PK/PD and safety** – Models of biodistribution, acute and sub-acute toxicity, and efficacy pertinent to the intended indication (e.g., tumor xenografts, antidiabetic models) [32].

Toxicological Profile: Safety and Adverse Effects

The three-month fresh juice (5% v/v) treatment did not alter the total number of red blood cells (RBC) and white blood cells (WBC), mean corpuscular hemoglobin (MCH), hemoglobin (Hb), mean corpuscular volume (MCV), and hematocrit (HCT), as well as levels of urea and sugar in mice and rats. The treatment did not alter the experimental subjects' behavior. The fruit's methanolic extract was safe and did not result in the death of guinea pigs, rats, or mice in amounts as high as 3.0 g/kg. Additional research conducted in rats, both male and female, found that the standardized fruit pulp of hydroalcoholic (70% ethanol) extract, when taken orally, was comparatively safe up to 1000 mg/kg. Seed extract with ethanol up to 5000 mg/kg did not cause harm to rats. Ethylhexylphthalate Di-2 extracted from this herb's fruit (18.3–75.5 mg/kg) is a widely used plasticizer that is harmful to human health [27].

Future Prospects

The nutritional value, health benefits, nutrient content of ash gourd and the plant's composition makes it valuable. Because of the multipurpose in nature, ash gourd is crucial for the production of food and medicine. It will be essential to create innovative uses of ash gourd in recipes for foods and medications, and industrial applications.[1]

CONCLUSION

Ash gourd has both therapeutic and nutritional benefits. Ash gourd is a rich source of a number of biologically active elements that support healthy health and lower the chance of contracting long-term illnesses like CVDs. Ash gourd is a special type of melon that has abundant in dietary fibers, flavonoids, and phenols. Polyphenols have a number of physiological effects, including immunomodulatory, antimicrobial, and antioxidant impacts. Moreover, ash gourd juice enhances intestinal health through altering the gut microbiota which has a vital role in human health.[37]

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