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Bioactivities of *Benincasa hispida*: Bridging Traditional Knowledge and Scientific Evidence

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Abstract

Benincasa hispida (family *Cucurbitaceae*), also known as winter melon, is one of the famous crops in Asian countries. It is mostly grown for its fruits. *B. hispida* is rich in phenolic compounds, flavonoids, and saturated and unsaturated fatty acids including palmitoleic acid, oleic acid, linoleic acid, stearic acid, α-linolenic acid, and others. Scientific exploration of *B. hispida* was driven by the traditional practice of the plant as a remedy for various pathological conditions. This paper describes the potential pharmacological activities of *B. hispida* contributed by a significant concentration of phytoconstituents. *B. hispida* extracts enhance bone formation and downregulate the bone-resorption activity. While the antimicrobial activities result from inhibition of efflux pump transporters on the surface of bacteria and support intracellular antibiotic accumulation to destroy the bacteria. The significant concentration of flavonoids and terpenoids in *B. hispida* extract also possesses anticrystallization activity, which further prevents the formation of urinary stones in urolithiasis conditions. *B. hispida* extract also provides neuroprotective effects by effectively scavenging reactive oxygen species (ROS) and reducing lipid peroxidation in neurodegenerative aging conditions. Besides, significant phytoconstituents from *B. hispida* extract provide a gastroprotective mechanism by increasing the gastric mucus secretion and strengthening the gastric mucosal barrier. *B. hispida* extract also suppressed T cell-mediated immune response in the inflammatory condition of arthritis to resolve the oedematous condition. Thus, the presence of these phytochemical constituents from *B. hispida* extract contributes to significant pharmacological activities.

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Introduction

The *Benincasa hispida* (Thunb.) Cogn. is a single species, monotypic genus in the big family of *Cucurbitaceae,* which is also commonly called the gourd family (Shyaula & Manandhar, 2021). *Cucurbitaceae* is coined by Liberty Hyde Bailey as cucurbits, and this terminology has been used for any species of the *Cucurbitaceae* family. In this family, genus Benincasa has only a single cultivated species, which is the hispida species, also sometimes referred to as cerifera. Hispida is carrying the meaning of hirsute pubescence on the plant foliage and unripe fruit, while cerifera refers to the presence of waxy cuticles on the mature fruit (Wehner et al., 2020; Narayana, 2021). *Benincasa hispida is* a monoecious climber, and it has yellow flowers, hairy stems, leaves, petals and young fruits. When the fruit matures, it is coated with white chalky wax and/or dense pelt minute hairs. The fruit flesh is white to pale-green, crisp, juicy and has week flavour. It also produces cylindrical or oval fruits and can reach a length of 15cm to 80 cm with a diameter up to 30cm (Swamy, 2022). Figure 1 showed the fruit and cross-section of *B. hispida* or winter melon fruit. *B. hispida* has separate male and female flowers on the same plants, and cross-pollination is conducted by insects. Its seeds are numerous, which are about 1 cm long and 6 mm wide. The seeds are edible and have a nutty taste once cooked. It has a slight odour which is comparable with the pulp and peels. The flower season is from May to June while the fruit season will begin from June until August (Behera et al., 2023).

Table 1: Taxonomic summary of *Benincasa hispida* (Thunb.) Cogn. (Singh et al., 2024).

Kingdom	Plantae
Phylum	Tracheophyta
Class	Magnoliopsida
Order	Cucurbitales
Family	*Cucurbitaceae*
Genus	*Benincasa*
Specie	*Benincasa hispida* (Thunb.) Cogn.

B. hispida is first to be cultivated in Southeast Asia where it is originally grown in China, India and is being distributed by navigators and missionaries to other parts of East Asia, which is Japan, Philippine, Malaysia, and Taiwan, and also being cultivated by Chinese immigrants in Bangladesh, Sri Lanka, Latin America and the Caribbean. Besides winter melon or ash gourd, several other names are referring to the similar plant given by the native community, such as *Fakwa, Funggwa, Mokwa, Dong Gua, Chamkwa* by Chinese, *Petha Kaddu, Boodagumbala, Kumbalanga, Neer Poosanikai, Boodida Gummadikaya* by Indian, *Koosmanda* in Sanskrit, *Pazadaba* by Persian, *Tougan* by Japanese, and *Tankoy* or *Kondol* by Filipino (Pessarakli, 2016; Boniamin et al., 2024).

Fig. 1: *Benincasa hispida* fruit and cross-section.

The terminology of ash or wax refers to waxy cuticles which presence on mature fruits, and it helps to increase the shelf life of the fruit after harvesting, to be kept throughout the winter season in certain countries. White powdery substance looks on the fruit surface resemble winter frost; hence, winter is adapted in the fruit name as winter melon. Around 98% of the fruit is edible and rich in water content, vitamins, fibres and minerals (Guo, 2015; Pessarakli, 2016). In Chinese herbal medicine, winter melon skin is commonly incorporated in cooking to relieve water retention with the symptoms of cold syndrome or heat syndrome, promotes urination, and promotes lactation in breastfeeding mothers (Hong, et al., 2022). The combination of winter melon with garlic sprout can be beneficial in relieving cough or asthma, while the soup of winter melon and snow fungus work for reducing oedema and high blood pressure. When winter melon is eaten together with shrimp or duck, this combination can promote good blood circulation, prevent anaemia and increase the growth of the skeleton. Moreover, according to *Sui Xi Ju Recipe* consumption of winter melon during pregnancy is beneficial to remove toxins and helps in nourishing the embryo (Guo, 2015). *Benincasa hispida* has long been valued for its medicinal and nutritional benefits. Accumulating scientific evidence indicates that its extracts are rich in bioactive phytoconstituents that underpin diverse biological activities. This review summarises the current understanding of the phytochemical profile of *B. hispida* extracts and critically discusses their biological significance, based predominantly on findings from in vitro and in vivo animal studies.

Anti-osteoporosis Activity

B. hispida fruit extract sample was studied for the effect on the proliferation and differentiation of osteoblasts and osteoclasts. In the bone modelling and remodelling process, the fundamental cells involved in the process include osteoblasts and osteoclasts, in which osteoblasts originate from macrophage lineage of hematopoietic stem cells, while osteoclasts originate from mesenchymal stem cells (Qin et al., 2020). In this process, osteoclasts are responsible for bone resorption, where between the bone matrix, osteoclasts secrete proteolytic enzymes and induce the breakdown of connective tissues in bones. Osteoclasts also secrete some acids which are responsible for dissolving minerals such as hydroxyapatite in some parts of the bones (Lee et al., 2021). In estrogen deficiency osteoporosis condition, alteration in serum biomarker RANKL/OPG ratio affects the bone remodelling process by increasing the activity of osteoclast and decreasing osteoclast apoptosis (Gosset et al., 2021). RANKL is a receptor activator of NF-kB ligand, which is secreted by preosteoblasts, osteoblasts, osteocytes and periosteal cells. RANKL will bind and activate RANK receptors on preosteoclasts and further stimulate the differentiation of preosteoclasts and increase osteoclast adherence on bone tissue (Tobeiha et al., 2020; Yadav et al., 2022). Meanwhile, osteoprotegerin (OPG) is also released by osteoblasts in order to modulate the differentiation of monocyte-to-osteoclast by taking part as a decoy receptor for RANKL and further inhibiting RANKL-RANK binding (Jiang et al., 2023). Thus, in estrogen deficiency conditions, the ability of estrogen to suppresses RANKL secretion and increases OPG production in osteoblasts diminished and result to increase in RANKL/OPG ratio to favour bone resorption (Simfia, 2020).

Meanwhile, a study conducted with the methanolic extract of *B. hispida* fruit to address the anti-osteoporotic effect on ovariectomy mice showed that supplementation of *B. hispida* fruit extracts has significantly reduced the level of serum RANKL and increased serum OPG level. These changes would further induce the RANKL/OPG ratio to favour bone formation and reduce bone resorption activity (Choi et al., 2022). The key constituent in *B. hispida* fruit extract that contributes to bone metabolism, particularly in estrogen-deficient conditions such as postmenopausal osteoporosis, is 2-furoic acid. 2-furoic acid has been shown to modulate bone metabolism by significantly influencing the balance between receptor activator RANKL and OPG, two critical regulators of bone remodelling (Choi et al., 2023). Studies have shown that 2-furoic acid influences this pathway by decreasing serum RANKL levels and increasing OPG levels. In an ovariectomized mouse model, supplementation with 2-furoic acid resulted in a significant reduction in serum RANKL and an increase in OPG levels as compared to untreated controls. This shift led to a decreased RANKL/OPG ratio, which favours bone formation over resorption (Choi et al., 2023). Hence, as illustrated in Figure 2, by modulating the RANKL/OPG pathway, the significant concentration of 2-furoic acid in *B. hispida* fruit extract enhances the proliferation of preosteoblasts and increases osteoblast differentiation, while inhibits the differentiation of osteoclasts which are responsible for bone resorption (Choi et al., 2022). Thus, this result suggested the ability of *B. hispida* fruit extract in enhancing bone formation with downregulate the bone-resorption activity of osteoclasts.

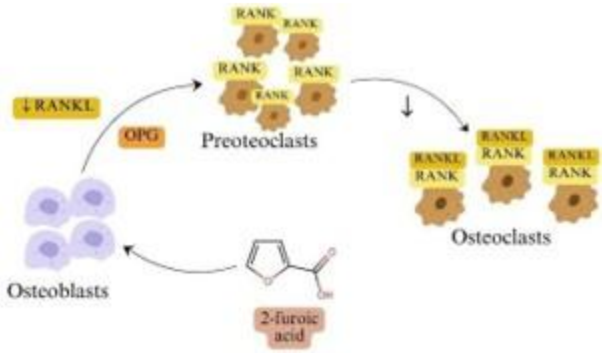

Fig. 2: Anti-osteoporosis activity in the presence of 2-furoic acid from *B. hispida* fruit extract.

Anti-microbial Activity

The search for alternatives to synthetic antibiotics in the treatment of infections is being explored through the study of natural antibacterial compounds in traditional medicines. These natural antibacterial compounds, namely tannins, polyphenols, flavonoids, saponins and alkaloids (Mazaya et al., 2020; Pikhtirova et al., 2023). Likely, the potential of antimicrobial activity of fruit extracts of *B. hispida* was studied with significant concentration flavonoid, tannins and polyphenols against pathogenic bacteria *(Bacillus subtilis, Sarcina lutea, Xanthomonas campestris, Escherichia coli* and *Pseudomonas denitrificans*) and fungi (*Fusarium oxysporum, Aspergillus niger* and *Collectotrichum melongenae*) (Biswas et al., 2021; Darmayani et al., 2021). The interaction of flavonoids in both Gram-negative and Gram-positive bacteria involved Inactivation of bacterial efflux pump transporters. These efflux pumps actively modulate solutes efflux from the cell and regulate the bacteria's internal environment to maintain membrane potential and extrude toxic compounds, including synthetic antibiotic which target the intracellular mechanisms. Hence, the inhibition of efflux pump transporters results in potential antibiotic activity as antibiotic intracellular accumulation occurs (Seukep et al., 2022). Besides, polyphenols and tannins, which are abundantly found in *B. hispida* fruit extracts, also exhibit antimicrobial properties by interacting with the bacterial cell membrane. Tannins have a strong affinity for bacterial cell membranes, which leads to changes in membrane potential and fluidity. This interaction can result in membrane disruption, increase membrane permeability and further causing intracellular contents leakage which ultimately leads to cell lysis. For instance, proanthocyanidins, condensed forms of tannins, can inactivate ATPase enzymes in the bacterial cell membrane and further compromise the membrane integrity, which promotes cell lysis (Czerkas et al., 2024). Meanwhile, polyphenols have a high affinity for cell wall components and alter the cell wall integrity. Polyphenols such as catechins bind to lipid head groups near the bilayer surface of bacterial cell membranes through hydrogen bonds. This binding will disrupt membrane integrity, which will lead to an increase in bacterial permeability and potentiate cell lysis (Olchowik- Grabarek et al., 2020; Xu et al., 2025). Collectively, these interactions disrupt bacterial membrane integrity, leading to increased permeability and potential cell lysis, hence contributing to the antimicrobial efficacy of *B. hispida* fruit extracts. The mechanisms of *B. hispida* fruit extract antibacterial activities were illustrated in Figure 3.

In a study, methanol peel and fruit extracts of *B. hispida* showed inhibition zone against *S.lutea, X. campestris* and *E. coli*. Next, peel extracts of ethyl acetate produced inhibition against *B. subtilis, S. lutea, E. coli,* and *P. denitrificans*, while fruit extracts inhibited *S. lutea, E. coli* and *P. dentrificans*. The extraction of *B. hispida* peel with chloroform solvent results in inhibition against *B. subtilis, S. lutea* and *E. coli.* Meanwhile, chloroform fruit extracts inhibited the significant diameter of *S. lutea* and *E. coli*. Besides, the antifungal activity of ethyl acetate peel extract results in a positive result against *Fusarium oxysporum* (Alam et al., 2021). Another study was conducted on the antibacterial activity against *Salmonella typhi* with chloramphenicol as a positive control. The study was conducted with four different concentrations of fruit extract; hence, the result showed that ethanol fruit extract has significant bioactivity against *Salmonella typhi*, and the effectiveness differ based on the fruit extract concentrations (Darmayani et al., 2021). Based on these studies, *B. hispida* fruits and peel extract may exhibit specialized antibacterial and antifungal activities against wide range of microorganisms.

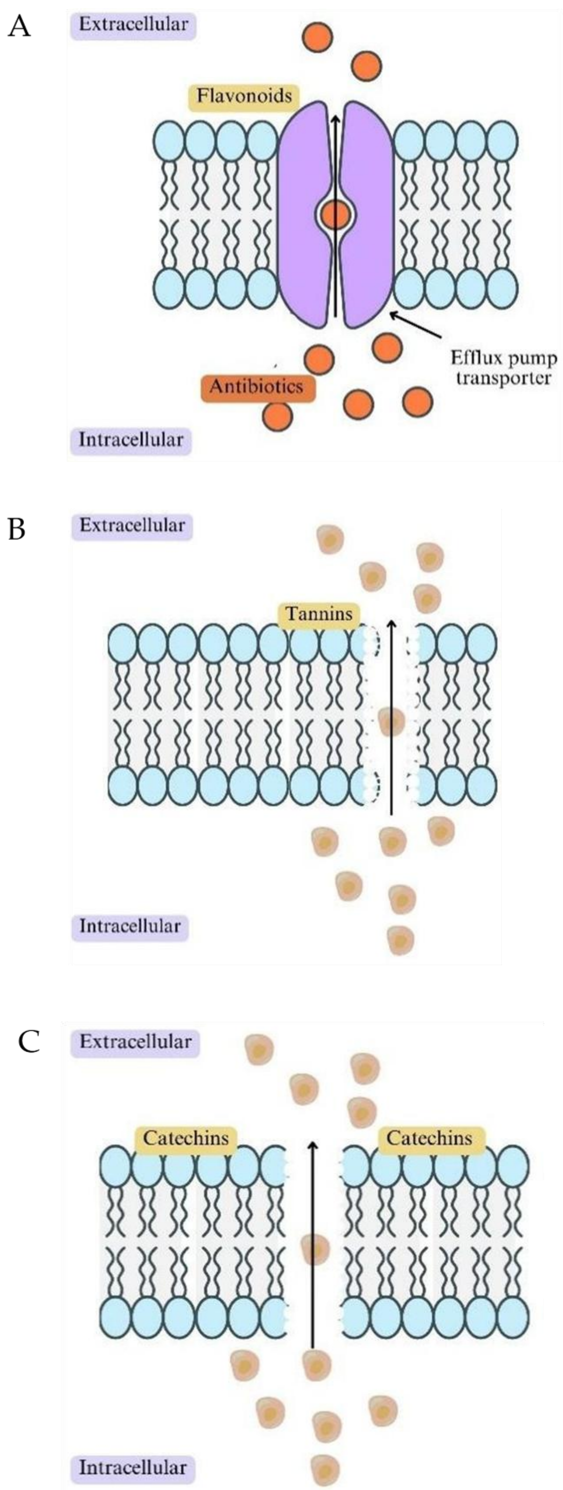

Fig. 3: The mechanism of *B. hispida* extracts antibacterial activities with (A) Flavonoids, (B) Tannins and (C) Catechins.

Anti-urolithiasis Activity

Urolithiasis is a condition where there is an accumulation of solute materials, and forming disturbing stones in either ureters or urinary bladder in any of the kidneys. The solutes material depends on urine concentration of calcium, oxalate, uric acid and phosphate (Skolarikos et al., 2022). The super-saturation of urine with these solutes becomes a crystallising factor and subsequently the growth factors for stone aggregation. Hence, a significant concentration of herbal extracts is possible to prevent super saturation or the initial stage of crystallisation in urolithiasis conditions (Nimavat et al., 2022).

In invitro study of anti-urolithiasis activity of *B. hispida* aqueous fruit extract, three different solvents, acetone, benzene and chloroform, were utilised to qualitatively study the phytochemical constituents which could inhibit the formation of oxalate crystals. Chloroform extract of *B. hispida* fruit presented a significant number of flavonoids, glycosides, terpenoids, carbohydrates and anthraquinones, which were found to develop higher capacity of calcium oxalate dissolution as compared to other extracts. The dissolution of calcium oxalate results with a significant crystal inhibition of calcium oxalate stone formation in the ureters or urinary bladder, which further reduces the occurrence of lithiasis (Susilo et al., 2021). Besides, the presence of terpenoids in the *B. hispida* fruit extracts possessed anti-crystallisation activity through disaggregation of crystallisation promoters (Rupali et al., 2021). The presence of a significant amount of terpenoids increase pH of the urine and increases urinary citrate (Sansores-España et al., 2022). The high citrate concentration in urine will inhibit crystal deposition and growth of renal stone in the renal tissue, besides, stimulate relaxation of smooth muscle of urothelium and facilitate urinary stone expulsion (Ghimire, 2019). The combination of all of these mechanisms, as illustrated in Figure 4, will reduce the potential of tubular damage and acute necrosis in the renal tissue. Thus, the *B. hispida* fruit extract with a significant concentration of flavonoids, glycosides, terpenoids, anthraquinones and triterpenoids could reduce and further prevent the formation of urinary stones.

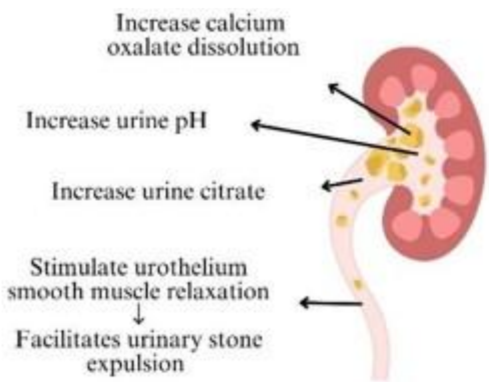

Fig. 4: The mechanism of anti-urolithiasis activities of *B. hispida* fruit extracts with different phytoconstituents.

Neuroprotective Activity in Ageing-Induced Neurodegeneration

One of the significant processes of ageing is neurodegeneration, which is due to a decline in various biochemical compositions. The susceptibility of the elderly with neurodegeneration is mainly a result of acceleration in oxidative stress and reactive oxygen species (ROS) activities (Oladele et al., 2021). A study of the effect of *B. hispida* fruit extract on the neurodegenerative disorder of albino mice, was conducted with observation on ROS activity. D-galactose was administered to alter brain biochemical markers (Ambikar & Mohanta, 2021). D-galactose oxygen metabolism results in the production of ROS, which causes neuronal damage, hence, results in neurodegenerative ageing-like symptoms such as learning and memory capacity impairments (Liu et al., 2020). D-galactose also reacts readily with free amine groups in proteins and peptides, which produce advanced glycation end-products (AGEs). Then, AGE-receptor binding and activation of the signalling pathway will generate more free radicals and cause oxidative stress. The increment in oxidative stress damages mitochondrial function and leads to less production of ATP and more production of free radicals (Kowalczyk et al., 2021). However, cotreatment of neurodegenerative conditions with *B. hispida* fruit extract improved the biochemical observation of cerebral cortex biomarkers. Also, a reduction in lipid peroxidation in *B. hispida* fruit extract illustrated a significant decline of oxidative stress activity, which is due to a reduction of ROS activity (Ambikar & Mohanta, 2021). As illustrated in Figure 5, the significant concentration of flavonoids such as quercetin in *B. hispida* fruit extract effectively scavenges ROS and reduces lipid peroxidation. This activity is due to the abundance of hydroxyl groups in flavonoids structure, which directly neutralises ROS and free radicals (Khan et al., 2021).

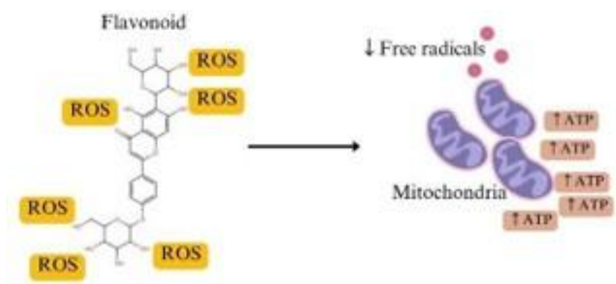

Fig. 5: The mechanism of flavonoids to neutralise ROS and reduce free radicals.

Besides, the chronic administration of D-galactose in this study also results in increased lipofuscin accumulation in the neural tissues, which also demonstrated accelerate aging symptoms. The buildup of lipofuscin is considered a hallmark of cellular ageing and is further associated with impaired cellular functions, which can contribute to neurodegenerative diseases (Ilie et al., 2020). Nevertheless, the presence of phenolic compounds and polysaccharides extracted from *B. hispida* fruit demonstrated the capability in preventing ROS production and further reducing oxidative damage that leads to lipofuscin formation. The notable reduction in lipofuscin accumulation after treatment with *B. hispida* fruit extract suggests that the extracts can preserve the neuronal function through enhancing antioxidant defences, reducing oxidative stress and inhibiting lipofuscin accumulation (Ambikar & Mohanta, 2021). Thus, the bioactive constituents in *B. hispida* fruit extracts contribute to the preservation of neuronal function and prevent neurodegenerative ageing symptoms.

Gastroprotective Activity

A peptic ulcer is a condition where there is an imbalance between gastric hydrochloric acid secretion and the maintenance of mucosal endogenous defense mechanisms (Jaiswal et al., 2021). The imbalance in gastric hydrochloric acid secretion may be due to stress-induced increase in hydrochloric acid secretion or stasis of acid, which further results in ulcer formation when the gastric lumen is exposed to the accumulating acid (Adebayo-Gege, 2023). Currently, the treatment of peptic ulcers includes H_2 and M_1-histamine blockers, proton pump inhibitors aiming to reduce gastric acid secretion, and sucralfate and carbenoxolone to provide protection on the gastric mucosal layer (Mehta et al., 2020; Djanaev et al., 2023). A study on the gastroprotective effects of *B. hispida* fruit was conducted with two extraction solvents, which are petroleum ether extract (PEBH) and methanol extract (MEBH). The qualitative phytochemical analysis showed that petroleum ether *B. hispida* fruit extracts (PEBH) mainly contained beta-sitosterol and lupeol, while methanol *B. hispida* fruit extract (MEBH) was rich in iso-vitexin. MEBH demonstrated better protection to reduce gastro-irritation caused by ethanol inducer. The ethanolic inducer increases mucus production, which protects the ulcer crater against the necrotic action of gastric acid and further provides significant reduction of ulcer craters in peptic ulcer conditions (Lebeau et al., 2021). MEBH and PEBH treatment on mice also illustrated better mucosal defense against the increase in acid and pepsin induced by pylorus, with a rise in the gastric mucus secretion, which acts as an effective mucosal barrier and prevents gastric ulceration (Singh et al., 2022). The extracts have also been shown to increase the production of gastric mucus, which serves as a protective barrier against irritants and pathogens. This mucus layer will prevent direct contact of harmful substances with the gastric epithelium and thereby reduce the risk of gastric ulcer formation (Islam et al., 2021).

In the stress-induced ulcers condition, the presence of flavone and sterols in MEBH and PEBH fruit extracts produces better gastroprotective activity through reduction in the generation of free radicals and lipid peroxidation, which indicates a decrease in oxidative degradation of lipids within the gastric mucosal cells. The preservation of cellular integrity strengthens the gastric mucosal barrier and maintains the stomach lining (Singh et al., 2022). These phytoconstituents contribute to the gastroprotective effects through their antioxidant and anti-inflammatory properties. Studies have reported that treatment with *B. hispida* fruit extracts leads to a significant increase in catalase (CAT) activity, which is an enzyme that is responsible for decomposing hydrogen peroxide into water and oxygen. This activity will prevent the potential oxidative damage within the gastric tissue. Additionally, fruit extracts have also been observed to enhance superoxide dismutase (SOD) levels, hence, contribute to the neutralisation of reactive oxygen species (ROS) in the gastric tissues (Rao et al., 2024; Cicio, 2025). Furthermore, *B. hispida* seeds and fruits extracts are also rich in flavonoids, which are favourable in gastric protection (Alsaadi et al., 2020). Flavonoids can inhibit gastric acid secretion by suppressing histamine H2 receptors and reducing proton pump activity in the gastric parietal cells. Histamine is released by mast cells as a biogenic amine that plays a vital role in increasing vascular permeability, smooth muscle contraction and gastric acid secretion. Whilst activation of mast cells involved elevation of intracellular Ca2+ levels as a prerequisite for the degranulation process, which in turn resulted to histamine release.

However, excessive histamine release in the gastric mucosa can lead to hyperacidity and contribute to the development of gastric ulcers. Hence, flavonoids have been shown to inhibit the increase of intracellular Ca2+ concentrations in mast cells upon activation and thereby reduce histamine release (Baran et al., 2023). As demonstrated in Figure 6, flavonoids also contribute to the stabilisation of mast cell membranes, which makes them less susceptible to activation and subsequent degranulation. The membrane-stabilising effect will further prevent the release of histamine and other pro-inflammatory mediators, which may worsen the gastric ulcer condition. The inhibition of histamine release will reduce histamine activation on H_2 receptors located on parietal cells of the stomach lining and further reduce gastric acid secretion (Engevik et al., 2020). This will prevent the risk of acid-related gastric mucosal damage due to hyperacidity and protect the gastric mucosa from ulcer formation.

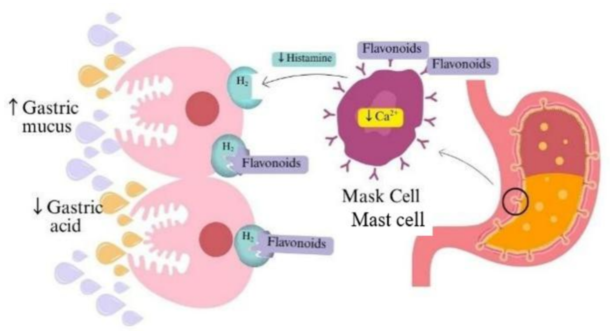

Fig. 6: Flavonoids mechanism in gastric parietal cells to stabilise gastric mucus acidity.

These combined actions contribute to the preservation of gastric mucosal integrity and offer a natural therapeutic approach for the prevention and treatment of gastric ulcers. Therefore, this study showed that *B. hispida* extract produced potent gastroprotective activity synergistically with maintaining gastric pH balance and inhibiting gastric acid secretion.

Immunomodulatory Activity in Arthritis

Rheumatoid Arthritis is an autoimmune disorder that is identified as chronic infiltration of synovium and leads to destruction of bone and cartilage (Fang et al., 2020). During joint inflammation, macrophage-like synoviocytes and fibroblast-like synoviocytes proliferate to form the pannus, and further invade and destroy the cartilage. These cells are also the major factor in promoting inflammation and joint destruction. While autoantibodies contribute to the inflammatory process as joint inflammation mediators and bone erosion (Cheng et al., 2022). In the treatment approach, the targeted cells pursued are T cells and B cells, proinflammatory mediators, and signalling molecules. This immunomodulatory activity is particularly beneficial in arthritis, whereas chronic inflammation plays a central role in joint damage and pain. The study of immunomodulatory activity of *B. hispida* seeds extract was conducted on mice, and *B. hispida* seeds extract was observed to provide a significant immunostimulation effect on arthritis induced condition in mice. The mouse paw volume was significantly reduced, which is indicating resolve in oedematous conditions as T cell-mediated immune response was suppressed after treatment with *B. hispida* seeds extract, hence reducing the overall inflammatory burden in arthritis conditions (Zhang et al., 2023).

Besides, post-treatment with *B. hispida* seeds extracts illustrated improvement in red blood cell (RBC) count, white blood cell (WBC) counts and haemoglobin (Hb) level, which indicated a good recovery from arthritis and anaemic condition (Atallah et al., 2024). The chronic inflammation arthritis condition often leads to anaemia of chronic disease (ACD), which is characterised by reduced RBC production and haemoglobin synthesis due to elevated iron regulatory hormone hepcidin levels, which inhibit iron absorption and recycling (Khalaf et al., 2019). Hence, *B. hispida* seeds extracts contained potent anti-inflammatory and antioxidant properties from active phytoconstituents such as flavonoids and phenolic acids to mitigate systemic inflammation and oxidative stress through suppressing the pro-inflammatory cytokines and enhancing antioxidant defenses. In this mechanism, the extract further reduces hepcidin overexpression and improves iron availability for erythropoiesis to restore RBC and Hb levels (Khalaf et al., 2019; Wang et al., 2022).

The histologic observation also revealed improvements in the arthritis condition, with a better profile of synovial membrane and fibrous tissues being detected on the transverse section of the knee joint. The *B. hispida* seeds extract, which contains high concentrations of linoleic acid and palmitic acid contributes to its ability to stabilise cell membranes and prevent the infiltration of inflammatory cells into synovial tissues. (Devidas Une et al., 2016). Thus, based on this study, *B. hispida* extract was proven to have a significant immunomodulatory effect in the treatment of arthritis conditions.

Conclusion

In conclusion, *Benincasa hispida* or winter melon is a useful phytoconstituents which provide various pharmacological benefits. Specifically, *B. hispida* extracts possessed significant anti-osteoporosis activity, antimicrobial, nephroprotective, neuroprotective, gastroprotective, and immunomodulatory activity in arthritis condition which were conducted in animal models. These pharmacological activities of *B. hispida were* reflected as the significant level of phytoconstituents, such as total phenolic compounds, flavonoids and fatty acids, were measured in the extracts. Thus, the concentration of phytoconstituents extracted greatly influences the pharmacological activity of the *B. hispida* extracts.

Although numerous studies have demonstrated the pharmacological potential of *Benincasa hispida*, several gaps remain in the current literature that warrant further investigation. Most existing studies have been conducted using in vitro and animal models; therefore, well-designed clinical studies are necessary to establish its efficacy and safety in humans. In addition, variations in extraction solvents, plant parts utilised, and phytochemical concentrations across studies make direct comparisons challenging. This underscores the need for standardized extraction and characterisation methods in *B. hispida* research.

Future studies should focus on the isolation and quantitative evaluation of key bioactive constituents responsible for the reported pharmacological activities, as well as elucidation of their underlying molecular mechanisms. Furthermore, continued exploration of *B. hispida* fruit—particularly its antioxidant, antimicrobial, anti-osteoporotic, anti-urolithiatic, neuroprotective, gastroprotective, and immunomodulatory properties—may expand its potential applications in functional foods, nutraceuticals, and pharmaceutical formulations. Comprehensive preclinical and clinical investigations are essential to validate its therapeutic efficacy and safety. Such efforts will facilitate the translation of *B. hispida* from traditional use into evidence-based medicinal and health-promoting products.

Authors contributions

Conceptualization, H.A.H., Z.I.S and U.S.M.H; writing—original draft preparation, U.S.M.H; writing—review and editing, H.A.H. and U.S.M.H; visualization, U.S.M.H; supervision, H.A.H. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest

There is no conflict of interest involved in the completion of this writing.

Declaration of generative AI and AI-assisted technologies in the writing process

During the writing of this paper the usage of AI or AI-assisted technologies was not involved.

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