

WITHANIA SOMNIFERA AND BACOPA MONNIERI -BASED POLYHERBAL GUMMIES: DEVELOPMENT, EVALUATION, AND THERAPEUTIC INSIGHTS

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ABSTRACT

The incorporation of traditional Ayurvedic botanicals with modern, patient-centric drug delivery systems offers significant potential for enhancing therapeutic compliance, particularly in the management of cognitive and neurological health. This review article outlines the development and evaluation framework for a novel polyherbal gummy formulation incorporating Bacopa monnieri (Brahmi) and Withania somnifera (Ashwagandha) as primary neuro-supportive agents, blended with Zingiber officinale (Ginger) and Cinnamomum verum (Cinnamon) to enhance bioavailability and provide supplementary antioxidant benefits. While conventional solid dosage forms often suffer from poor palatability and lower adherence among paediatric and geriatric populations, chewable medicated gummies offer a highly palatable, water-independent alternative. This paper comprehensively reviews the pharmacological profiles of the selected phytoconstituents, focusing specifically on their neuroprotective, anxiolytic, anti-inflammatory, and bioavailability-enhancing properties. Furthermore, it outlines a systematic, theoretical methodology for formulating these polyherbal gummies using a gelatin and agar-agar polymer matrix. The review also details standard quality control and evaluation parameters necessary for future empirical studies, including physical stability, moisture content, pH, syneresis, and in-vitro dispersion time. Ultimately, this approach bridges the gap between established polyherbal phytotherapy and modern nutraceutical delivery, providing a foundational blueprint for the future laboratory development and clinical evaluation of medicated gummies.

KEYWORDS: Brahmi, Ashwagandha, Polyherbal Gummies and Therapeutic insights.

INTRODUCTION

The oral route is the most widely accepted method of drug administration due to its cost-effectiveness, simplicity, and high patient compliance. However, conventional tablets or unpalatable syrups can lead to non-compliance, particularly in paediatric populations. Gummies offer an extended residence time in the oral

cavity and provide a convenient alternative to measuring liquid formulations or swallowing intact solid dosage forms.^[1]

Medications are formulated to treat illnesses, prevent diseases, and ensure human safety in daily life. Modern medical research widely employs various herbal

formulations to support human health, representing a core component of traditional healthcare in many Asian nations. The World Health Organization estimates that 80% of the population in several Asian and African countries relies on herbal medicine for their primary healthcare and treatments.

Herbal formulations consist of specific dosage forms containing one or more herbs, blended in precise amounts to offer nutritional, cosmetic, or therapeutic benefits. Medicinal plants remain a vital source for pharmaceutical development, with numerous plant-based substances currently undergoing early research and clinical trials. Herbal medicines are utilized for both prophylactic and therapeutic purposes, generally presenting fewer side effects than conventional allopathic drugs.

This review outlines the therapeutic benefits of these medicinal plants and provides a clear overview of herbal medicine. These remedies are highly advantageous due to their safety, tolerability, efficacy, and minimal side effects. India holds a rich heritage of traditional medicine, including officially recognized systems such as Ayurveda, Yoga, Unani, Siddha, and Homeopathy.^[2]

When multiple herbs are combined into a single medicine, it is termed a Polyherbal Formulation (PHF). Blending herbs with diverse beneficial active ingredients can produce highly effective treatments, particularly for enhancing human nutrition. These mixtures are favoured for their broad therapeutic window, meaning they remain safe at higher doses and exhibit minimal toxicity.^[3]

Gummies, sometimes known as jellies, are semisolid, oil-free, transparent or semi-transparent oral formulations prepared with water-soluble bases like gelatin, pectin, tragacanth, alginate, and boro-glycerine. They possess appealing organoleptic properties and are easy to swallow, making them an ideal choice for children, elderly, and patients suffering from dysphagia. Upon chewing, the formulation mixes with saliva and can be rapidly absorbed through the oral mucosa, accelerating the onset of action and partially bypassing hepatic first-pass metabolism.^[4]

Active ingredients for gummies

1. Brahmi

- Biological Source: It is obtained from the fresh and dried whole plant of *Bacopa monnieri* (L.) Wettst.
- Family: Plantaginaceae
- Synonyms: water hyssop, brahmi, thyme leafed gratiola pennywort, herb of grace, Indian pennywort.
- Chemical constituent: Bacoside, Bacopaside, Bacopasaponin, Cucurbitacin.

Brahmi is a brain herb utilized to remove body toxins, enhance memory, improve concentration, and aid in overcoming addictions.^[5]

Uses

Learning and memory: The nerve-damaging chemical colchicine led to a drop in acetylcholine, reduced the activity of acetylcholinesterase, and lowered the binding of muscarinic cholinergic receptors in the frontal cortex and hippocampus. Applying *Bacopa monnieri* for two weeks successfully reversed these negative effects. It has been suggested that a decline in noradrenergic function can help offset the behavioural impacts of cholinergic damage. Because *Bacopa monnieri* is known to boost 5-hydroxytryptamine levels and lower norepinephrine in the cerebral cortex, hypothalamus, and hippocampus, it indirectly changes acetylcholine concentrations.^[6]

Anti-inflammatory: *Bacopa monnieri* can lower inflammation by altering the release of chemicals that cause inflammation. It possesses powerful anti-inflammatory qualities, which might explain its effectiveness in traditional medicine for treating various inflammatory conditions. Furthermore, it significantly lowered the activity of the enzymes cyclooxygenase-2 (COX-2), 15-LOX, and 5-lipoxygenase (5-LOX). Its triterpenoid and bacoside components are likely responsible for this beneficial activity.

Anti-epileptic/Anti-convulsive activity: Ayurvedic medicine recommends *Bacopa* as an epilepsy treatment, and animal studies have proven it has anticonvulsant qualities, provided it is taken in large amounts over a long period. Furthermore, research has shown that the raw water extract of *Bacopa monnieri* controls epilepsy in laboratory animals. It naturally produced a calming effect and significantly prolonged the sleep-inducing action of phenobarbitone. It is widely understood that medications that boost GABA provide calming, pain-relieving, and anticonvulsant benefits. This suggests that the central nervous system is regulated by the GABA-ergic system. The impacts of *Bacopa monnieri* on the passive avoidance task, maximum electroshock seizures, and movement in mice were evaluated both by itself and alongside phenytoin (PHT). Both the acquisition and retention of memory improved without interfering with phenytoin's ability to stop convulsions. Further studies using *Bacopa monnieri* alone or combined with other anti-seizure drugs are needed to completely explore its potential against epilepsy.

Antioxidant: The alcoholic and hexane extracts of *Bacopa monnieri* show antioxidant properties by stopping lipid peroxidation. A newer study looked at how *Bacopa monnieri* acts as an antioxidant through other pathways, like blocking the activity of glutathione peroxidase (GPX), catalase (CAT), and superoxide dismutase (SOD). In the nitro blue test, researchers also saw that the hydroalcoholic extract of the entire *Bacopa monnieri* plant reduced the amount of superoxide created by polymorphonuclear cells. Because the methanolic extract of *Bacopa monnieri* can directly stop the creation of the superoxide anion in a dose-dependent manner, it lowers nitric oxide (NO) levels. Activated astrocytes

produce nitric oxide both with and without enzymes, and this molecule might be involved in several brain-degrading diseases, such as Alzheimer's disease, ischemia, and epilepsy.

Anti Stress Anxiolytic Activity (Medhya): The standardized extract of *Bacopa monnieri* possesses adaptogenic qualities. Taking a low dose of *Bacopa monnieri* extract beforehand significantly reversed changes in the ulcer index and plasma AST alone, while a larger dose significantly reversed changes in the ulcer index, adrenal gland weight, CK, and AST. The anxiety-reducing effects of higher *Bacopa monnieri* extract doses were noticeably more potent than those of lorazepam (LZP). However, *Bacopa monnieri* holds a clear advantage over lorazepam because it enhances memory in humans and animals without causing amnesia. Shanker and Singh also observed these results and concluded that the *Bacopa monnieri* extract provided an anxiety-reducing effect.

Anti-depressant Activity: The methanolic extract of *Bacopa monnieri* may offer antidepressant benefits in rodents. When given orally for five days at 20 and 40 mg/kg doses, the extract demonstrated strong antidepressant effects in forced swim and learned helplessness depression models. This level of activity was similar to that of the drug imipramine.

Anti-Asthmatic Activity (Kasahara Shwasahara): The extract of *Bacopa monnieri* showed relaxing effects in the tracheal muscles of rabbits and guinea pigs, with prostaglandins and beta-adrenoreceptors playing a small part. Additionally, it triggered bronchodilation in anesthetized rats, supporting the plant's historical use for various respiratory issues. The extract's ability to open airways might be shown by its opposition to the effects carbachol has on inspiratory and expiratory pressures. The extract impacted carbachol-induced airway tightening in two ways: it mostly reduced inspiratory pressure at lower doses (25 and 37 mg/kg), but only reduced expiratory pressure at a high dose (50 mg/kg). This trait of the plant extract implies that several different mechanisms might cause this bronchodilation. Potential causes include the activation of beta-adrenoreceptors, blocking of muscarinic receptors, release of prostaglandins, or interference with calcium movement. A more recent study by the same authors demonstrates that the ethanol extract of *Bacopa monnieri* contains calcium-blocking activity. Additionally, researchers noted that the methanolic extract of *Bacopa monnieri* acted as a strong mast cell stabilizer, implying that *Bacopa monnieri* leaves could help treat allergic diseases.

Anti-Cancer Activity (Ayushya / Vayastha): Giving *Bacopa monnieri* beforehand to malignant patients significantly lowered the acute stress-induced increases in the ulcer index, adrenal gland weight, plasma glucose, aspartate aminotransferase (AST), and creatine kinase

(CK). This positive result was caused by the anticancer qualities of the bacosides present in *Bacopa monnieri*. The methanolic extract demonstrated powerful mast cell stabilizing effects. Because it is known to heavily absorb cadmium, chromium, lead, and mercury, *Bacopa monnieri* is used as a plant-based remedy.

2. Ashwagandha

- Biological Source: It is obtained from the dried roots and stem bases of *Withania somnifera* Dunal.
- Family: Solanaceae
- Synonyms: Indian Ginseng, Winter Cherry^[7]
- Chemical constituent: Withanolide, Alkaloids, Flavonoids, Withanolide glycosides, Sterols, Chlorogenic Acid, Coumarins, Saponins, Resins, Carbohydrates, Fatty Acids^[8]

Uses^[8]

Anticancer (Breast Cancer): Breast cancers tend to be very aggressive and spread easily due to their highly diverse structure. Ashwagandha impacts breast cancer cells by triggering programmed cell death at the molecular level, specifically apoptosis. Researchers have discovered that ashwagandha could treat breast cancer, especially the triple-negative and estrogen receptor/progesterone receptor (ER/PR) positive types.

Alzheimer's Disease: The brain shows an abnormal buildup of β -amyloid protein as Alzheimer's disease gets worse. In its fibrillar form, it exerts a nerve-damaging effect by breaking down glucose transport in nerve cells and creating free radicals, which harm and kill cells. Certain studies were done on human nerve cells. Ashwagandha has been shown to neutralize the damaging effects of β -amyloid in cells, a factor that might add to cognitive decline during HIV infection. A study used rats that were orally given vitanon, an ingredient extracted from the root of *Withania somnifera*. The blocking of amyloid b-42 was tied to major improvements in cognitive function, along with a drop in lipid peroxidation, nitric oxide, and the inflammation-promoting cytokines TNF- α , IL-1 β , IL-6, and MCP-1. Furthermore, withaferin A, which comes from Ashwagandha, looks like a promising substance for treating Alzheimer's disease. It works by stopping the buildup of tau proteins and lowering b-amyloid clumping. Moreover, withaferin A manages the production of heat shock proteins (HSPs) that increase during stress, and it blocks oxidative and inflammation-causing chemicals. Still, more research is needed to check if withaferin A is safe and to prove its nerve-protecting benefits in treating Alzheimer's disease. Researchers tested *Withania somnifera* derivatives to see how they affect the formation of β -amyloid 42 deposits in Alzheimer's disease. They found that the water-repelling core of β -amyloid1-42 interacted with withanolide A, withanolide B, withanoside IV, and withanoside V as an oligomer, which stops further interaction with monomers and reduces clumping.

Parkinson's Disease: The main characteristic of Parkinson's disease, a progressive age-related nerve-degrading illness, is the loss of dopamine-producing substantia nigra neurons caused by a mix of environmental and genetic factors. This condition is connected to unusual protein clumping, mitochondrial problems, and oxidative stress. Researchers discovered that the ethanolic root extract from Ashwagandha can reverse Parkinson's-like symptoms in Parkinson's disease caused by MPTP. A study was conducted on rats where Parkinson's disease was triggered by 6-hydroxydopamine. Ashwagandha was found to increase glutathione levels, reduce lipoperoxidation, and boost the activities of glutathione S-transferase, glutathione reductase, glutathione peroxidases, superoxide dismutase, and catalase, alongside increasing catecholamines, dopamine D2 receptor binding, and tyrosine hydroxylase expression. When compared to the control group, treating the mice suffering from Parkinson's disease with Ashwagandha extract improved their biochemical markers and reduced their motor problems.

Huntington's Disease: Huntington's disease is a worsening nerve-degrading condition characterized by oxidative stress and the death of nerve cells in the basal ganglia. It is an inherited autosomal dominant syndrome associated with dementia, emotional instability, and muscle problems. It also includes difficulties with speech, language, and movement, as well as depression, short-term memory loss, and a lack of focus and concentration. Inducing the condition with nitro propionic acid mimics Huntington's disease-like abnormalities, especially oxidative stress, unusual walking patterns, and mitochondrial problems. Inhibiting complex II causes further changes in behaviour, enzymes, and biochemistry. Additionally, reports show that the GABAergic system is involved in the development of Huntington's disease. Thanks to its GABAergic effects and antioxidant qualities, Ashwagandha can help treat Huntington's disease by restoring glutathione and acetylcholinesterase enzyme levels and improving cognitive function.

Anti-depressant Activity: Depression is a complex disorder mainly linked to brain health through mood swings, thoughts, bad behaviour, disappointments, sadness, hopelessness, a loss of physical activity, and low self-esteem. Furthermore, depression is connected to changes in eating and sleeping habits and other daily tasks, on top of anxiety symptoms. Experimental studies show that Ashwagandha can assist people dealing with depression. In the year 2000, Bhattacharya and his team isolated the bioactive glycowithanolides from Ashwagandha roots and tested their potential as an antidepressant at 20 and 50 mg/kg doses. They discovered that glycowithanolides provided an antidepressant effect similar to imipramine during behavioural despair and learned helplessness caused by a forced swim test.

3. Ginger

- Synonyms: Rhizoma zingiberis, Zingibere
- Biological Source: Ginger consists of the dried rhizomes of the *Zingiber officinale* Roscoe
- Family: Zingiberaceae.
- Chemical Constituents: α -zingiberol; α -sesquiterpenealcohol α -bisabolene, α -farnesene, α -sesquiphellandrene. Less pungent components like gingerone and shogaol are also present.^[9]

Uses

Anti-oxidant Activity: Any disruption to the cell's antioxidant defence system can cause an overproduction of Reactive Oxygen Species (ROS) and ultimately increase oxidative stress. Researchers have studied many natural antioxidants for their ability to neutralize free radicals and fight oxidative stress to prevent health problems and restore normal levels of both. A living organism relies on keeping a normal ROS level to function properly, which can be done by giving free radicals hydrogen atoms or electrons to stop ROS production and turn them into thermally stable products or antioxidant lipid complexes. Over the last 20 years, finding natural plant resources has become more popular and widely used, likely due to their bio actives, lower toxicity, and cheaper production costs. The significant antioxidant capacity in ginger's bioactive substances can help restore or maintain regular oxidative stress levels. Reports show that the antioxidative potential of ginger leaves is higher than that of its rhizomes and flowers. 6-gingerol demonstrated a stronger in vitro antioxidant activity ($88.93 \pm 0.03\%$ DPPH; $88.23 \pm 0.98\%$ ABTS). Giving mice oral 6-gingerol (50-75 mg/kg body weight) every day for three weeks improved insulin signalling, reduced oxidative stress, and increased blood glucose levels. For DPPH and ABTS, the matching antioxidant activity of shogaols was $90.2 \pm 0.11\%$ and $89.01 \pm 0.6\%$. Because it has a unique functional group called an α , β -unsaturated carbonyl that effectively controls glutathione, 6-shogaol boasts the strongest antioxidant capacity compared to other ginger phenols. Glutathione is the most common type of thiol in animal cells, and it plays a role in intracellular redox regulation and the cell's detoxification process against harmful chemicals.

Anti-Inflammatory Activity: The body uses inflammation as a step in its natural healing process to fight off invaders and stop injuries or infections. The main goals of inflammation are to prevent cell damage, clear away dead cells and tissues, and restore stability to the inside of the cell. Severe inflammation stimulates cells to produce inflammatory interleukins, cytokines, and tumour necrosis factors, including inflammation-boosting cytokines like tumour necrosis factor α (TNF- α), interleukin- 1β (IL- 1β), and interleukin-6 (IL-6), because many mononuclear immune cells enter the area. A new study on ginger's anti-inflammatory traits shows that eating ginger can greatly lower serum levels of TNF- α while barely affecting IL-6. Furthermore, because 10-gingerol possessed a stronger anti-neuroinflammatory

effect than ginger's other active ingredients, the study showed that the anti-neuroinflammatory power of gingerols grew as the alkyl chain length got longer. In addition, other live animal studies have backed up these claims by proving how useful ginger bio actives are. When given orally to mice with acute and chronic colitis at a dose of 0.3 mg/mice daily for a week, ginger nanoparticles effectively stopped intestinal inflammation by lowering pro-inflammatory cytokines like TNF- α , IL-1 β , and IL-6 and raising levels of anti-inflammatory cytokines like IL-10 (interleukin-10) and IL-22 (interleukin-22). When mice with colitis caused by dextran sulphate sodium were given 6-shogaol-equipped nanoparticles (equal to 15 mg/kg of 6-shogaol) orally every day for a week, they not only experienced fewer colitis symptoms but also healed faster.

Anti-microbial Activity: Natural and organic antimicrobials sourced from plants, animals, and microbes are currently replacing chemical and synthetic antimicrobials in both food preservation and health management. These biologically derived antimicrobials from plant sources are favoured for their lower toxicity, reduced drug resistance, and multi-targeted treatment approach. Researchers have evaluated the impressive antibacterial, antiviral, and antifungal properties of ginger and its derivatives. Microorganisms frequently use biofilm formation as a defence mechanism against antimicrobials. A study by Chakotiya et al. shows that ginger stops the creation of biofilms and disrupts membrane stability in *Pseudomonas aeruginosa*, a bacterial strain resistant to multiple drugs. Ginger essential oil displays excellent antibacterial activity against food-borne illness-causing microbes, including *Staphylococcus aureus* and *Escherichia coli*. A study revealed that the bactericidal action of ginger essential oil destroys cell membrane activity and interferes with energy metabolism due to certain large molecular components like proteins and nucleic acids. Another study noted that fresh ginger oil had a moderate antimicrobial effect on *Candida*, *Bacillus subtilis*, *Trichoderma* spp., and *Penicillium* spp., while showing no inhibition against *Aspergillus niger*, *P. aeruginosa*, and *Saccharomyces cerevisiae* showed a modest effect. Researchers showed that dried ginger oil had stronger antibacterial action against *P. aeruginosa*. Because blocking antioxidant activity might help retain antibacterial activity, antioxidant and antibacterial qualities are closely connected. Processing and storage could also change ginger's functional qualities, which would in turn alter its antibacterial and antioxidant properties.

Anti-Carcinogenic: Cancer was one of the leading causes of death globally in 2020, with roughly 10 million of the 19 million reported cases being fatal. In recent years, researchers have heavily studied ginger's anticarcinogenic properties against various cancers, such as colorectal, prostate, breast, and cervical cancers. Chronic inflammation plays a major role in

carcinogenesis because it is closely connected to all the critical stages of cancer formation. Ginger and its active ingredients have been shown to protect against all phases of cancer development, including its start, promotion, advancement, and resistance to medication. An in vitro study showed that a polyphenol-rich fraction from dried ginger powder stopped the growth of colorectal and stomach adenocarcinoma cells. Researchers conducted both in vitro and in vivo studies to evaluate ginger's toxic effects on cells and its method of acting against prostate cancer. A paper stated that 6-gingerol, 6-shogaol, 10-gingerol, and 10-shogaol showed strong anti-proliferative effects on human prostate cancer cells by altering the expression of the proteins GST π (glutathione-S transferase) and MRP1 (multi-drug resistance associated protein 1). Combining ginger bioactives like 6-gingerol, 8-gingerol, 10-gingerol, and 6-shogaol synergistically reduced the spread of PC-3 prostate cancer cells. 6-Gingerol caused human gastric adenocarcinoma (AGS) cells to create more ROS, which decreases the mitochondrial membrane potential and triggers cell death. Applying 10-20 μ M of 6-shogaol in vitro to PC12 cells for 24 hours improved the phase II antioxidant compounds in the mouse pheochromocytoma cell line and successfully stopped PC12 cells from multiplying under oxidative stress. On the other hand, 6-gingerol could not protect the PC12 cells from oxidative stress, which might have been due to the absence of an α , β -unsaturated ketone, indicating that this unit is important for protecting cells.

Neuroprotective Activity: The development of nerve-degrading disorders, like Parkinson's and Alzheimer's, is possible, making older individuals especially vulnerable. According to many recent studies, ginger could help treat and prevent neurodegenerative illnesses due to its anti-neuroinflammatory properties and its important role in memory function. Furthermore, a lipopolysaccharide-activated BV2 microglia culture test showed that 10-gingerol from fresh ginger had strong anti-neuroinflammatory qualities. By stopping NF- κ B activation, gingerol restricted the expression of inflammation-causing genes, which then led to a decrease in IL-6, IL-1 β , NO, and TNF- α levels. At a 20 μ M concentration, ginger-based phytochemicals like shogaols and gingerols have proven to have strong neuroprotective properties, especially against Alzheimer's disease. Ginger might reduce A β -species and brain plaques, stop brain inflammation, change tau protein, and limit apoptosis caused by A β through multiple pathways.

Cardiovascular Protection: Cardiovascular disease accounts for 17.9 million deaths a year, making it the top cause of premature death worldwide. Many studies have demonstrated that ginger successfully lowers blood pressure and blood cholesterol levels, providing protection against cardiovascular illnesses. Mice that were fed a high-fat diet with 0.5% freeze-dried ginger extract for about two weeks experienced weight loss and

an increase in serum levels of high-density lipoprotein cholesterol (HDL-C), which is called good cholesterol because it protects against heart diseases. Ginger extract also encouraged the creation of high-density lipoproteins (HDL) by increasing the liver's levels of apolipoprotein A-1 and lecithin cholesterol acyltransferase RNA. Another study proved that ginger extract can reduce total cholesterol and low-density lipoprotein (LDL). Combining aerobic exercise with a daily oral dose of liquid ginger extract (250 mg/kg of feed) for about a month raised HDL levels in rats on a high-fat diet.

Anti-Obese Activity: Obesity, or being overweight, is a significant global issue caused by disruptions in energy metabolism. Based on their structure and behaviour, adipose (fat) tissues can be split into two groups. White adipose tissues mostly act as energy storage, while brown adipose tissues are responsible for boosting metabolism and burning energy. Converting white adipose tissues into brown ones is an innovative way to fight obesity. 6-Gingerol might encourage cell browning in 3T3-L1 adipocytes through a process that relies on AMPK. Researchers found that gingerenone A stopped adipogenesis and fat formation more effectively than gingerol and shogaol in 3T3-L1 preadipocyte cells. Giving gingerenone A (50 mg/kg of body weight) orally every day for 15 weeks also influenced fatty acid metabolism by activating AMPK in vivo, which impaired diet-induced obesity.

Anti-Diabetic Effect: Diabetes mellitus is a chronic metabolic condition characterized by insulin resistance or lack of insulin, which leads to an uncontrollable rise in blood glucose levels. Chronic high blood sugar might encourage advanced glycation end products (AGEs) and protein glycation. An in vitro study found that 6-gingerol and 6-shogaol restricted methylglyoxal (MGO), the precursor to AGEs, to prevent AGEs from forming and slow the development of diabetes complications. Mice with Type 2 diabetes were given a daily oral supplement of 6-gingerol (200 mg/kg of corn oil) for 28 days. This treatment increased glycogen storage in skeletal muscles by boosting glycogen synthase 1 and enhancing the presence of the GLUT4 (glucose transporter type 4) cell membrane.^[10]

It is also used as: Anti-bacterial, Anti-fungal, Anti-allergic, Anti-emetic, Hepatoprotective, Bronchoprotective, Anti-hypertensive, Radioprotective, Flavouring agent.^[11]

4. Cinnamon

- Synonym: Cinnamomum Zeylanicum
- Biological source: Dried inner bark of genus Cinnamomum
- Family: Lauraceae
- Chemical constituents: Cinnamaldehyde, cinnamic acid, coumarin, catechin, etc.^[12]

Uses

Diabetes: Diabetes mellitus is a chronic glucose metabolism condition caused by insulin resistance and malfunctioning beta cells in the pancreas. Diabetes is a serious medical issue that affects people of all ages and genders across the globe. Cinnamon has been shown to possess insulin-mimicking qualities because its active ingredients boost glucose absorption by triggering insulin receptor kinase activity, insulin receptor autophosphorylation, and glycogen synthase activity. One study demonstrated that a compound extracted from cinnamon, called methyl hydroxyl chalcone polymer, boosted insulin-dependent glucose metabolism in vitro by roughly 20 times. According to Safdar et al., methyl hydroxyl chalcone polymer made fat cells more responsive to insulin by activating the enzyme that helps insulin attach to cells and by blocking the enzyme that stops the maximal phosphorylation of the insulin receptor, a process linked to higher insulin sensitivity. A 12-week regimen of 500 mg/d of cinnamon, which is rich in polyphenolic components, was shown to improve impaired fasting glucose and lower oxidative stress. Another study revealed that consuming 500 mg/d of a specific water-based cinnamon extract (Cinnulin PF) for 12 weeks greatly improved several metabolic syndrome factors, including body composition, systolic blood pressure, and fasting blood sugar. Because metabolic syndrome is linked to cardiovascular disease, these results could have a major impact on public health.

Anti-cholesterol: The components in cinnamon have been proven to enhance blood lipid profiles, insulin control, and glucose absorption. A study focused on patients with type 2 diabetes who consumed cinnamon. The results showed that people who took 1 g, 3 g, or 5 g of cinnamon for 40 days saw significant drops in fasting serum glucose (18-29%), triglycerides (23-30%), total cholesterol (12-26%), and low-density lipoprotein cholesterol (7-27%).

Antioxidant: Cinnamon has polyphenols, which are natural dietary antioxidants proven to block 5-lipoxygenase and thereby reduce oxidative stress in a dose-dependent manner. Cinnamon holds several specific antioxidant phytochemicals, including camphene, eugenol, gamma terpinene, phenol, salicylic acid, tannins, and epicatechin. Natural antioxidants are currently gaining a lot of attention, and efforts are underway to replace synthetic ones. Additionally, people can prevent oxidative body damage by adding these natural antioxidants to functional diets.

Cancer: Effective cancer-fighting medicines have been derived from plants, and 60% of today's market anticancer drugs come from natural sources like microbes, plants, and marine life. Researchers have heavily studied herbs with anticancer properties and have used them as strong anticancer medications. Cinnamon's anticancer qualities have recently been shown to halt the growth of several human cancer cell lines, such as lung,

ovarian, breast, and leukaemia tumour cells. It is widely known that metastasis, one of the primary causes of cancer-related death, involves cell adhesion, invasion, and migration. One study examined how cinnamon extract affected the movement of SiHa (human cervical carcinoma) cells. The findings showed that cinnamon greatly reduced the migration of cancer cells, indicating it could serve as an anticancer medication for cervical cancer. Cinnamon extract, which mostly contains cinnamaldehyde and a mix of polyphenols, has a therapeutic effect on cervical cancer cells by depolarizing the mitochondrial membrane potential and causing the cells to die. A different study showed that cinnamon extract stops hematologic malignancy cells from multiplying. Moreover, applying cinnamon extract to melanoma cell lines reduced the expression of Cox-2 and HIF-1 α in tumour tissues, factors that normally facilitate cinnamon's strong anticancer action. It is well established that Cox-2 and HIF-1 α act as key regulators to worsen angiogenesis and metastasis during cancer. Research on effective anticancer drugs supports using herbal medicine. Still, before herbal medicine can be used as an anticancer therapy, a lot of research and strict standards for toxicity, safety, quality control, standardization, and clinical trials are required.

Angiogenesis inhibitor: Angiogenesis is the process tumours use to build new blood vessels to promote their growth and spread. VEGF is one of the most vital and specific angiogenesis factors. Clinical trials are currently reviewing and testing various strategies to suppress VEGF. Anti-VEGF medications currently on the market have shown serious adverse effects, including perforation, bleeding, and gastrointestinal hypertension. Because they are safe for humans to use, there is renewed interest in discovering natural anti-VEGF medicines. Eating a plant-based diet has also proven useful in preventing cancer development. One study notes that cinnamon is a natural dietary source of anti-VEGF compounds. It demonstrated that cinnamon and its components (like tetrameric procyanidins and type A procyanidin trimer) effectively blocked both VEGF signalling and VEGFR2 kinase activity in endothelial cells. Cinnamon extract reduced multiple features of angiogenesis in mice, such as the growth and movement of endothelial cells and the formation of tumour-induced blood vessels. More research is needed to pinpoint the main factors responsible for cinnamon extract's antiangiogenic effect. As a natural VEGFR2 inhibitor, cinnamon extract could become a standard dietary approach to preventing and treating cancer.

Alzheimer's disease: Alzheimer's disease (AD) is a progressive, neurodegenerative, and irreversible brain disorder characterized by memory loss, confusion, poor judgment, and a loss of language skills. Many studies have shown that the buildup of soluble oligomeric assemblies of β -amyloid polypeptides, or amyloid-beta ($A\beta$), heavily influences the development of AD. Numerous studies have shown that compounds from

natural sources can stop the formation of $A\beta$ plaques. A study indicates that cinnamon extract stops $A\beta$ from harming neuronal PC12 cells and blocks the creation of toxic $A\beta$ oligomers. Another study discovered that giving cinnamon extract orally to a model of aggressive AD transgenic mice improved their cognitive behaviour and reduced plaques. Based on the findings, using natural substances like cinnamon helps stop the formation of harmful oligomeric $A\beta$ species in AD. AD can arise from intracellular tau neurofibrillary tangles and extracellular plaques (like $A\beta$). Tangles are important in the progression of neurodegeneration and form later on compared to amyloid production. The goal of most drugs used to prevent or treat AD is to inhibit cholinesterase function or amyloid plaque development. Compounds that can stop tau from clumping together may have a major impact on creating new medications. Tau is a protein with prominent polyrich sections that show little to no structure under normal conditions. When researchers investigated the effects of an aqueous cinnamon extract containing proanthocyanidins on tau aggregation, they found that both the proanthocyanidin trimer and cinnamaldehyde in the extract were responsible for effectively inhibiting human tau aggregation in vitro.

Anti-gastric ulcer: *Helicobacter pylori* is largely responsible for peptic ulcers, stomach cancer, and chronic gastritis. Probiotic microorganisms have been used to strengthen the immune system, prevent inflammatory bowel diseases, lower the risks of cancer and mutations, and suppress *H. pylori* and intestinal infections. Yogurt containing *Bifidobacterium* and *Lactobacillus acidophilus* can stop *H. pylori* growth in clinically infected patients. Behrad et al. showed that, compared to liquorice and control yogurt, cinnamon yogurt had the strongest inhibitory effect on *H. pylori* growth in vitro for both tested strains. The study states that cinnamon preparations historically used for gastrointestinal issues effectively reduce *H. pylori* with little to no side effects. The strong anti-*H. pylori* action of these formulations might solve the problem of antibiotic treatment resistance. Simethicone is the most common drug used to treat dyspepsia. A study shows that a cinnamon stomachic mixture can cut dyspepsia symptoms by 70% and works similarly to simethicone. People consider the cinnamon stomachic combo to be safe, effective, and affordable compared to simethicone. Using it for a longer period can also increase the favourable response by up to 80%.

Antibacterial, antifungal: Cinnamon oil is the oil with the highest potential for bactericidal effects. Cinnamon oil has proven to possess antibacterial properties. Whether used alone or mixed with triclosan, gentamicin, or chlorhexidine, it effectively stops the formation of biofilms, breaks apart existing biofilms, and kills bacteria within the biofilms of clinical *Staphylococcus epidermidis* strains. The fact that bacteria do not build resistance to essential oils might be another reason why

they are better than antibiotics. More research is needed to completely understand the complex way cinnamon and its components act against *S. epidermidis* biofilms and other medically important microorganisms. Cinnamaldehyde is one of the main ingredients in cinnamon oil. Research shows that cinnamaldehyde drains intracellular ATP levels and destroys the cytoplasmic membrane in both Gram-positive and Gram-negative bacteria. Cinnamaldehyde stops the proliferation of fungi like yeasts, filamentous molds, and dermatophytes, as well as the eggs and adults of human head lice (*Pediculus humanus capitis*). Alcohol and water extracts of cinnamon have also displayed antibacterial action against *Helicobacter pylori*. The hardwood species *Osteophloeum cinnamomum*, known as the "indigenous cinnamon tree" or kaneh (*Lauraceae*), possesses strong antifungal properties. The endemic *C. osmophloeum* tree grows in Taiwan's natural hardwood forest, and its leaves contain essential oils with chemical components identical to *C. cassia* bark oil. Essential oils from *C. osmophloeum* leaves heavily inhibited fungal growth. The primary chemical in these leaf essential oils, cinnamaldehyde, showed the strongest antifungal properties compared to the other constituents. People can easily collect the leaves without debarking the trees to gather a large amount of natural bioactive essential oils or cinnamaldehyde; this could eventually result in the production of fumigants or wood preservation agents.

Nematicidal: People are increasingly worried about how pesticides affect human health and the environment, and how repeatedly applying chemical pesticides can unintentionally harm nontarget organisms. Natural alternative sources like plant essential oils have been suggested because they break down into harmless compounds and have a minimal negative impact on the environment and nontarget creatures. In Japan and North America, the pine wood worm, *Bursaphelenchus xylophilus*, is linked to dead or dying conifers like pines. One study evaluated the nematicidal properties of four cinnamon oils and two cassia oils; the results showed they are effective against adult *B. xylophilus* and could serve as a good natural control agent. The study states that cinnamaldehyde is the most hazardous chemical against adult *B. xylophilus*, followed by (E)-2-methoxycinnamaldehyde and (E)-cinnamic acid.

Acaricidal and repellent effect: House dust mites (*Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*) are a primary cause of allergies in human homes, leading to symptoms like atopic dermatitis, asthma, perennial rhinitis, and even sudden infant death syndrome. Controlling mite species involves using chemical methods or treatments with repellents like DEET and benzyl benzoate. However, repeatedly using these compounds has caused resistance to emerge and raised concerns about their potential impact on human health. Because the allergen comes from the dead bodies or faeces of dust mites rather than the living mites themselves, repelling them is more effective than killing them. To manage house dust mites, it is better to seek out natural repellents, including plants packed with various bioactive compounds. Researchers have tested pure cinnamon essential oil for its ability to repel and kill house dust mites. It proved to be a highly effective material for this specific purpose. Using it might also reduce chemical resistance and negative health consequences.^[13]

It is also used as: Anti-bacterial, Anti-inflammatory, Anti-oxidant, Immune booster, Flavouring agent.

5. Honey

- Synonyms: Madhu
- Biological source: It is a saccharine fluid (from the nectar of flower) deposited in the honey comb by the hive bee, *Apis mellifera*, *Apis dorsata* and other species of *Apis*.
- Family: Apidae.^[14]
- Chemical constituents: Glucose, fructose, sucrose, dextrin, formic acid.

Uses

Sweetening agent, Anti-inflammatory, Antibacterial, Antimicrobial.

6. Other ingredients used in gummies

- **Gelatine and Agar-Agar**
Purpose: Texture, chewiness, structure, shape, mouthfeel, stability
- **Orange juice**
Purpose: pH adjuster, flavour enhancer, synergy with other ingredients.
- **Sodium benzoate**
Purpose: preservative, prevents microbial growth.^[12]

Table 1: Role of ingredients used in gummies.

Ingredients	Role of ingredients
Brahmi	Active ingredient
Ashwagandha	Active ingredient
Cinnamon	Flavouring agent
Ginger	Flavouring agent
Honey	Sweetening agent
Orange juice	Vehicle and flavouring agent
Gelatine	Gelling agent
Agar-agar	Thickening agent
Sodium-benzoate	Preservative

Procedure

Begin with thoroughly cleaned and dried glassware. Place 50ml of orange juice into a water bath. While stirring continuously, add the agar-agar, honey, and gelatine, heating the mixture to 70-75°C. Subsequently, stir in the ashwagandha powder until the formulation is completely smooth and uniform. Once fully blended,

pour the liquid mixture into gummy molds. Allow the molds to cool at room temperature for 30 minutes, then transfer them to a refrigerator for 24 hours to set completely. After 24 hours, remove the jellies from the molds and store them in a closed container under refrigerated conditions.

Table 2: Amount of ingredients used in gummies.

Ingredients	F1	F2	F3
Brahmi	2.5g	2.0g	1.5g
Ashwagandha	2.0g	1.5g	1.0g
Cinnamon	3.5g	3.0g	2.5g
Ginger	3.0g	2.0g	1.5g
Honey	25g	10g	10g
Orange juice	50ml	50ml	50ml
Gelatine	10g	10g	10g
Agar-agar	5g	5g	5g
Sodium-benzoate	0.1g	0.1g	0.1g

EVALUATION PARAMETERS OF GUMMIES

1) Physical Evaluation: The gummies are visually and sensorially assessed for characteristics including colour, odour, texture, taste, shape, and transparency.

2) Stickiness and Grittiness: The gummy is evaluated by gently rubbing it between the fingers to check for excessive stickiness or particulate grittiness.^[15]

3) pH: A 1% solution is prepared by dissolving 0.5g of the jelly in 50ml of distilled water. The pH is measured at room temperature using a digital pH meter, as it influences both the flavour and stability of the formulation.^[16]

4) Stability: The gummies are stored under refrigerated conditions at 4°C for 4 weeks to monitor their physical integrity over time.

5) Solubility test: The solubility of the formulation is tested by dissolving portions in water, ethanol, ether, and 0.1 N HCl.

6) Microbial examination: The melted gummy base is smeared onto a sterile petri dish and incubated at 37°C for 24 hours to observe any bacterial or fungal growth.

7) Moisture content: 10g of crushed gummies are dried in a hot air oven at 105°C until a constant weight is achieved to determine the percentage of water loss.

8) Weight variation: Ten individual gummies are weighed to determine their average weight, ensuring uniformity across the batch.

9) Syneresis: The gummies are stored at room temperature (25°C ± 5°C) and under refrigeration (8°C ± 1°C) to check for the exudation or leakage of water from the gel matrix. Syneresis formulations were rejected and not chosen for additional research.^[4]

10) Dissolution: USP paddle device is used in in-vitro dissolution studies, filled with 900 ml dissolution media maintained at 37°C ± 0.5°C and 50 rpm. After 10, 20, 30, 40, 50, 60, 90, or 120 minutes, 5 ml of the sample can be removed, and the sink condition can be maintained by replacing that sample with fresh 5 ml medium. Drug content can be determined using a UV spectrophotometer. % drug release can then be computed. Due to the extremely diverse ingredients, dissolution testing of polyherbal medication becomes challenging. Dissolution technique development is significantly more difficult than it is for a defined single constituent since the contents of polyherbal medicinal goods sometimes include a mixture of several herbal constituents.^[17]

11) Disintegration test: Disintegration tests can be utilised as an alternative to in vitro dissolving studies for polyherbal jellies. Six jellies are placed in a disintegration apparatus containing 0.1N HCl maintained at 37°C ± 0.5°C, and the time required for complete breakdown is recorded.^[17]

12) Dispersion time test: A gummy is added to 100ml of purified water at 37°C under constant stirring. The optimal dispersion time for the formulation should fall between 10 to 30 minutes.^[18]

CONCLUSION

The formulation of polyherbal gummies incorporating Brahmi and Ashwagandha represents an effective and modern approach to supporting cognitive health. By transforming these traditional Ayurvedic botanicals into an appealing, chewable gummy, patient compliance can be greatly improved, particularly among demographics that struggle with conventional solid dosages. While this study establishes the theoretical formulation and evaluation framework, further laboratory testing, stability studies, and clinical trials are required to validate the

safety and efficacy of these gummies in real-world applications.

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