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BRAHMI AND SHANKHAPUSHPI-BASED POLYHERBAL GUMMIES: DEVELOPMENT, EVALUATION, AND THERAPEUTIC INSIGHTS

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ABSTRACT
This review summarizes the formulation and evaluation of polyherbal gummies incorporating Brahmi (*Bacopa monnieri*), Shankhpushpi (*Convolvulus pluricaulis*), ginger, cinnamon, honey, and supportive excipients to deliver a palatable, geriatric- and paediatric-friendly dosage form aimed at cognitive support and allied health benefits. The article outlines roles of actives and auxiliaries, proposes three prototype formulations (varying herb loads, sweetener levels, and spices), and details a hot-processing workflow using orange juice as a vehicle with gelatine and agar-agar as dual gelling systems to optimize texture, stability, and acceptability. A comprehensive quality evaluation plan is provided, covering organoleptic properties, stickiness/grittiness, pH, stability, solubility profiling, microbial examination, moisture content, weight variation, syneresis, and performance tests such as dissolution, disintegration in 0.1 N HCl at 37 ± 0.5 °C, and dispersion time benchmarking against chewable gummy standards. The rationale integrates literature on the nootropic, anxiolytic, antioxidant, anti-inflammatory, antimicrobial, and gastrointestinal benefits of the botanicals, aligning with current innovations in functional gummies and mixed gelling systems to improve compliance and early onset via buccal exposure while minimizing first-pass loss. Overall, the work provides a pragmatic framework for polyherbal gummy development and quality control suited to nutraceutical and pediatric/geriatric use-cases.
Keywords- Brahmi, Shankhapushpi, Polyherbal Gummies and Therapeutic insights

INTRODUCTION

Any medication designed to treat illnesses, prevent them, or ensure human safety in daily life is considered a herbal medication. Herbal medicines are an important part of the traditional human health care system of an Asian nation. Modern medical research and technology employ a variety of herbal medication formulations in various dose forms for human healthcare. According to estimates from the World Health Organisation, 80 percent of people in various Asian and African nations currently utilise herbal medicine for primary healthcare and treatment purposes.

Herbal formulations are dosage forms that contain one or more herbs or a combination of herbs in prescribed amounts to offer particular nutritional, cosmetic, or supplemental advantages.

An essential source for the production of pharmaceuticals is medicinal plants. Numerous substances obtained from herbal sources are presently undergoing preclinical research and clinical trials. Herbal medicine is used for both prevention and treatment, and it includes everything from the use of standardised and treated herbal extract to traditional and popular medicine in every nation. Herbal medications have fewer adverse effects than allopathic ones. The study aims to explain the therapeutic efficacy of the different drugs and gives a comprehensive overview of herbal medicine.In the daily lives of human science, herbal medicine has more benefits than allopathic medicine. because they have greater safeguards, improved tolerance, less side effects, and high potency and efficacy. Ayurveda, Yoga, Unani, Siddha, and homeopathy are the official traditional medical systems of India, where a number of traditional healthcare systems have been practiced for centuries.[1]

The process of preparing herbal medicine by combining multiple herbs is known as Polyherbal Formulation (PHF).

Two or more herbs with diverse phytoconstituents and comparable or dissimilar medicinal potential make up the Poly Herbal formulation. When it comes to controlling human nutrition, several herbs combine to produce positive results. Polyherbal formulations' remarkable therapeutic range—that is, their capacity to be safe at large dosages while causing few adverse effects when taken in excess—has contributed to their immense popularity.[2]

Gummies, sometimes known as jellies, are semisolid, oil-free, clear or semi-transparent medicines that can be applied topically or taken internally. Oral gummies are made from water-

soluble bases such tragacanth, gelatine, pectin, alginate, and Boro glycerine. Furthermore, this medication looks nice, which makes it more useful for both elderly and younger patients. Oral gummies are also accepted by individuals with dysphagia as well as by the elderly and young. Both local and systemic therapy can be applied to the oral cavity. By using saliva instead of water and allowing for quick drug absorption through the buccal mucosa, oral gummies speed up the breakdown of medications while reducing the first-pass effect.Compared to the pills that are currently available on the market, it offers a significantly earlier start of action and more efficient drug absorption.[3]

The oral route of medicine administration is the most widely used because of its inexpensive treatment costs, ease of administration, patient compliance, and formulation flexibility. For children, the traditional dosage forms—such as tablets, capsules, syrups, etc.—are inconvenient. people due to the bad taste of the medication or the difficulty swallowing pills and capsules. Consequently, the need to create new technologies has been growing daily. Gummies are intended to enhance oral retention time, patient compliance, and acceptance. Particularly with padeatrics, they are typically seen to be more handy than syrups or pills. While syrups may need to be measured and poured, which may be messy and time-consuming, gummies are simple to chew and consume.[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 herb of grace ,indian pennywort.
- Chemical constituent: Bacoside, Bacopaside , Bacopasaponin, Cucurbitacin.

Brahmi is the most important nervine herb. It helps to remove toxins from body. It improves memory and enhances the ability of concentration while reducing the blockage present in nervous system. Brahmi help us to give up on bad habits and addictions.[5]

Uses

Learning and memory - The neurotoxic, colchicines, caused acetylcholine depletion, decreased acetylcholinesterase activity, and decreased muscarinic cholinergic receptor binding in the frontal cortex and hippocampus. These effects were reversed by administering BM for two weeks. It has been proposed that a decrease in noradrenergic function can mitigate the behavioral effects of cholinergic degeneration. Since BM is known to enhance 5-hydroxytryptamine levels and decrease norepinephrine in the cerebral cortex, hypothalamus, and hippocampal regions, it indirectly alters Ach concentrations[14].

i. **Anti-inflammatory**: By modifying the release of pro-inflammatory mediators, bacopamonnieri can reduce inflammation. It has strong anti-inflammatory properties, which may be related to how effectively it works in traditional medicine to treat a variety of inflammatory illnesses. Additionally, it markedly reduced the activities of cyclooxygenase-2 (COX-2), 15-LOX, and 5-lipoxygenase (5-LOX). Its triterpenoids and bacosides may be the cause of this activity.

ii. **Anti-epileptic/Anti (Apasmaraghna) convulsive Activity**: Ayurvedic medicine has suggested bacopa as a treatment for epilepsy, and animal studies have demonstrated that it possesses anticonvulsant properties, but only when taken in large quantities over an extended length of time. Additionally, it has been revealed that BM's crude water extract regulates epilepsy in test animals. It naturally had a sedative effect and greatly extended phenobarbitone's hypnotic action. It is well recognized that drugs that increase GABA have calming, pain-relieving, and anticonvulsant properties. It implies that the central nervous system is mediated by the GABA-ergic system. BM's effects on the PA task, maximum electroshock seizures, and locomotor activity in mice were assessed both alone and in conjunction with phenytoin (PHT). Without influencing PHT's anticonvulsive action, memory acquisition and retention both improved. To fully investigate the potential of BM in epilepsy, more research utilizing BM alone or in conjunction with other antiepileptic medications is necessary.

iii. **Antioxidant:** By preventing lipid peroxidation, BM's alcoholic and hexane extracts exhibit antioxidant qualities. A more recent study

investigated the antioxidant impact of BM through additional mechanisms, such as the inhibition of glutathione peroxidase (GPX), catalase (CAT), and superoxide dismutase (SOD) activities. In the nitro blue experiment, it was also noted that the whole BM plant's hydroalcoholic extract inhibited the amount of superoxide generated from polymorphonuclear cells. Because BM's methanolic extract can directly and dose-dependently inhibit the formation of superoxide anion, it lowers nitric oxide (NO) concentrations. NO is produced by activated astrocytes both enzymatically and non-enzymatically, and it may play a role in a number of neurodegenerative diseases, including AD, ischemia, and epilepsy.

iv. Anti Stress – Anxiolytic Activity (Medhya) - BM's standardized extract has adaptogenic properties. Changes in ulcer index and plasma AST alone were considerably reversed by pretreatment with a low dose of BM extract, while changes in ulcer index, adrenal gland weight, CK, and AST were significantly reversed by pretreatment with a larger dose. The anxiolytic effects of the higher doses of BM extract were noticeably stronger than those of LZP. However, BM has a clear benefit over lorazepam (LZP) because it promotes memory in both humans and animals and does not cause amnesia. Shanker and Singh also noted these outcomes and concluded that the BM extract had an anxiolytic effect.

v. Anti depressant Activity - In rodents, BM methanolic extract may have antidepressant properties. The extract was found to have strong antidepressant action in forced swim and learned helplessness models of depression when administered orally for five days at doses of 20 and 40 mg/kg. This activity was comparable to that of imipramine.

vi. Anti-Asthmatic Activity (Kasahara Shwasahara) In the tracheal muscles of rabbits and guinea pigs, BM extract demonstrated relaxing qualities, with prostaglandins and (beta)-adrenoreceptors playing a minor role. Additionally, it caused broncodilation in rats under anesthesia, which confirmed the plant's traditional use for a number of respiratory conditions. Bronchodilator property of extract may be reß ected by antagonism of carbachol generated effects on inspiratory and expiratory pressures. The extract had a twofold effect on carbachol-induced bronchoconstriction. mainly inhibited inspiratory pressure at low dosages (25 and 37 mg/kg), but only inhibited expiratory pressure at high doses (50 mg/kg). This characteristic of the plant extract suggests that broncodilation may be caused by many mechanisms of action. Activation of (beta) adrenoreceptors, antagonism of muscarinic receptors, release of prostaglandins, or disruption of calcium mobilization are a few of the potential causes. The same authors' more recent investigation shows that the ethanol extract of BM contains calcium antagonistic action. Furthermore, it has been noted that BM methanolic extract demonstrated a strong mast cell stabilizer, suggesting that BM leaves may be beneficial for allergic diseases.

vii. Anti–Cancer Activity (Ayushya / Vayastha) - In malignant patients, pretreatment with BM significantly decreased the rise in ulcer index, adrenal gland weight, plasma glucose, aspartate aminotransferase (AST), and creatine kinase (CK) brought on by acute stress (AS). This was brought on by the anticancer properties of the bacosides found in BM. Strong mast cell stabilizing action was demonstrated by the methanolic extract. Known to hyperaccumulate cadmium, chromium, lead, and mercury, bacopamonneri is utilized as a phytoremedy.

2) Shankhpushpi

- Biological Source: It is obtained from the fresh and dried whole herb of Convolvulus pluricaulis.
- Family: Convolvulaceae
- Synonyms: Sankhaphuli, Shankhini
- Chemical constituent :Shankhapushpine, Convolamine, Scopoletin, Ceryl alcohol,β-sitosterol.

It is medicinally used for a brain tonic, nervine tonic. The entire aerial plant is used and reported to be tasteless to somewhat bitter while being traditionally used in the form of a decotion with cumin and milk .The plant itself called as Aloe weed in English. [5]

Uses:

i. Antidepressant activity - One of the rare medications that was utilized as an antidepressant and to induce a stress-free state in the brain was Shankhpushpi. Research conducted on animals under stress revealed that Shankhpushpi possesses antidepressant and stress-relieving qualities. There is still more

research to be done on the process of stress reduction.

ii. **Effects on Learning and Memory -** Simple memory tests like the tube climber, passive avoidance paradigm tests, and the active avoidance test have clearly shown improvements in memory after taking Shankhpushpi extracts. The ability of CP's ethanolic extract, ethyl acetate, and aqueous fractions to improve memory was investigated. Animal groups were given different amounts of ethyl acetate and aqueous portions of ethanolic extract (100 and 200 mg/kg/po). All CP extracts at both dosages markedly enhanced the rats' capacity for memory and learning.

iii. **Antimicrobial, insecticidal, antifungal, antibacterial and anthelmintic activity -** Using Spilosoma obliquo Walker as the test insect and a food repellent, the entire plant was biologically examined using the leaf disk method. Tetratriacontenoic acid was found in this plant for the first time, but 29-oxodotriacontanol, a novel chemical that was isolated from the chloroform fraction of this plant, was found to be a powerful anti-nutritional element in laboratory trials. As references, neem and azadirachtin crude extracts were utilized. At an 8000 ppm concentration, the novel chemical 29-oxodotriactanol produced an 85.74% inhibition. Convolvulus pluricaulis's alcoholic extract exhibited potent antifungal properties.

iv. **Anticonvulsant effect -** The alcoholic extract's water-soluble component inhibits the fight response and spontaneous motor activity, but it has no effect on the flight response; Electrically Provoked Convulsions The extract prevented tremor-induced tremors and epileptic seizures. Animals given methanolic extracts of stem callus, leaf callus, and entire plants (200 mg/kg orally) demonstrated exceptional protection against tonic seizures brought on by transcorneal electric shock. These results are also comparable to those of the common medication phenytoin. Strong antispasmodic effects have also been demonstrated.

v. **Antiulcer and anticatatonic effects** It was discovered that mucosal development was the cause of this plant's antiulcer properties. Glycoprotein, mucosal cell longevity, and mucin production are examples of defensive factors rather than offensive ones like acid pepsin.

vi. **Cardiovascular activity -** The sum The plant's water-soluble part impaired the function of the frogs' heart muscles and produced severe, prolonged hypotension in dogs. entire plant extract with ethanol. Mammals' and amphibians' cardiac muscles are negatively ionotropically affected. It also caused smooth muscle to spasmolyze.

vii. **Hypolipidemic -** ethanolic extract from whole plants when given to gerbils fed cholesterol. After 90 days, there was a noticeable drop in triglycerides, phospholipids, LDL cholesterol, and serum cholesterol.

viii. **Effect on the reproductive system and immunomodulation -** The plant's whole sap inhibits heavy menstruation. The plant can be ground into a fine paste that can be used to treat abscesses.

ix. **Traditional Uses of Clematis Pluricaulis in India -** In India, the herbs have been used for millennia to treat a variety of ailments, including anxiety and sleeplessness, as well as to increase longevity and stave against illness by boosting immunity. It heals intestinal worms, painful urination, animal poisoning, shortness of breath, cough, diabetes, and uterine disorders. It also improves strength, digestion, complexion, and voice. Hematemesis, heart disease, sleeplessness, and epilepsy can all benefit from it. The leaves and blossoms are used to treat anxiety neuroses and have antihypertensive qualities. According to the tribes of Chhindwara, Madhya Pradesh, India, it is an anthelmintic, a herb that treats skin conditions, decreases high blood pressure, and is beneficial for dysentery. The leaves are used in Gonda, Uttar Pradesh, India, to treat depression and mental illnesses. The herb is non-toxic, and there are no negative effects from using it. It has a stimulating influence on weight gain and health, however. Rasayana therapy, in accordance with the Ayurvedic idea, improves both the body and the mind simultaneously. This treatment boosts the body's resilience to illness, improves IQ, and delays the consequences of aging.It is among the most significant Medhya Rasayana medications in Ayurveda. In addition to having an astringent and bitter impact, using it helps to balance and correct Kaphavata-Pitta dosha imbalances. According to herbalists, Shankhpushpi soothes the nerves by controlling the body's synthesis of the stress chemicals cortisol and adrenaline.

x. **Antiaddictive Effect -** The antiaddictive properties of Shankhpushpi churan (powder) were investigated in mice with alcohol addiction. It revealed antiaddictive potential and shown an effective effect on cortico-hippocampal GABA levels. impact on memory and learning Research on the effects of streptomycin-induced memory impairment using a polyherbal formulation containing Convolvulus pluricaulis. Over the course of the 14-day observation, cholinergic behavior improved and oxidative stress decreased. Convolvulus pluricaulis, commonly referred to as a cognitive booster, was the subject of a study conducted on the Canscora decussta variety. The plant's ethanolic extract significantly increased nerve growth factor, which may be the cause of the cognitive power enhancement. According to Indian custom, children are given Shankhpushpi, a reliable natural cure, along with cow's milk or honey to help them remember things better. For developing children, these natural compounds serve as both a dietary supplement and an adjuvant. It is also possible to generate a potentiated Bhavita dosage form of Shankhpushpi [by following the traditional recommendations of Bhavana (levigation/wet grinding)] and explore its bio-potential in memory enhancement. While the safety assessment of recently created dosage forms should be closely monitored, efforts should also be made to prepare green manufactured metallic nanoparticles utilizing Shankhpushpi extract and investigate its biological properties in various neurological illnesses accordingly.

xi. **Antioxidant effect -** Due to the presence of flavonoids, alkaloids, and glycosides, the study conducted on the aqueous extract of Convolvulus pluricaulis shown a substantial antioxidant effect by scavenging the free radicals in stressed-induced circumstances. Convolvulus pluricaulis methanolic extract demonstrated an antioxidant activity by scavenging free radicals.

xii. **Anti-inflammatory and antipyretic effect -** Convolvulus pluricaulis ethanolic extract shown a notable antipyretic and mildly anti-inflammatory activity. [16]

Ginger

- **Synonyms** : Rhizomazingiberis, Zingibere
- **Biological Source**: Ginger consists of the dried rhizomes of the Zingiberofficinale Roscoe
- **Family** : Zingiberaceae.

Chemical Constituent: α-zingiberol; α-sesquiterpenealcohol α-bisabolene, α-farnesene, α-sesquiphellandrene. Less pungent components like gingerone and shogaol are also present.[6]

Uses:

i. **Antioxidant Activity -** The overproduction of Reactive Oxygen Species (ROS) and, ultimately, an increase in oxidative stress can result from any disruption or modification to the cell's antioxidant defense system. Numerous natural antioxidants have been studied for their ability to neutralize free radicals and combat oxidative stress in order to prevent various health issues and restore normal levels of both. A living organism's ability to function normally depends on maintaining a normal ROS level, which can be accomplished by giving free radicals hydrogen atoms or electrons to prevent the production of ROS and turn them into thermally stable products or antioxidant lipid complexes. The discovery of natural plant resources has grown in popularity and use over the last 20 years, most likely as a result of bioactives, reduced toxicity, and cheaper production costs. Significant antioxidant capacity in ginger bioactive substances can help restore or maintain normal levels of oxidative stress. According to reports, the antioxidative potential of ginger leaves is higher than that of ginger rhizomes and flowers. 6-gingerol was shown to have a greater in vitro antioxidant activity (88.93 0.03% DPPH; 88.23 0.98% ABTS). For three weeks, mice were given oral 6-gingerol (50–75 mg/kg body weight) every day, which improved insulin signaling, decreased oxidative stress, and raised blood glucose levels. For DPPH and ABTS, the corresponding antioxidant activity of shogaols was 90.2 0.11% and 89.01 0.6%. Compared to other ginger phenols, 6-shogaol has the strongest antioxidant capacity because it has a unique functional group called -unsaturated carbonyl, which effectively regulates glutathione. The most abundant form of thiol in animal cells is glutathione, which is involved in intracellular redox regulation and the cell detoxification process against harmful chemicals.

ii. **Anti-Inflammatory Activity -** The body uses inflammation as a stage in its normal healing process to fight off invaders and stop injuries or infections. Inflammation's primary goals are to prevent cellular damage, remove and absorb necrotic cells and tissues, and restore the

intracellular environment's stability and conformance. The production of inflammatory interleukins, cytokines, and tumor necrosis factors, including inflammation-promoting cytokines like tumor necrosis factor α (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6), is stimulated when cells undergo severe inflammation because many mononuclear immune cells are penetrated. According to a new study on ginger's anti-inflammatory properties, eating ginger can significantly reduce serum levels of TNF-α while having little effect on IL-6. Additionally, as 10-gingerol had a stronger anti-neuroinflammatory effect than the other active ingredients in ginger, it was shown that the anti-neuroinflammatory potential of gingerols increased as the alkyl chain length increased. Additionally, other in vivo investigations have substantiated these assertions by demonstrating the usefulness of ginger bioactives. By lowering pro-inflammatory cytokines like TNF-α, IL-1β, and IL-6 and raising levels of anti-inflammatory cytokines like IL-10 (interleukin-10) and IL-22 (interleukin-22), ginger nanoparticles, when given orally to mice with acute and chronic colitis at a dosage rate of 0.3 mg/mice daily for a week, effectively stopped intestinal inflammation. When 6-shogaol-equipped nanoparticles (equal to 15 mg/kg of 6-shogaol) were given orally every day for a week to mice with dextran sulfate sodium-induced colitis, they not only reduced the symptoms of the colitis but also accelerated the healing process.

iii. Antimicrobial Activity - In both food preservation and health management, natural and organic antimicrobials produced from plants, animals, and microbes are currently replacing chemical and synthetic antimicrobials. Because of their decreased toxicity, drug resistance, multi-targeted strategy, and multi-oriental treatment, these biologically derived antimicrobials from plant sources are favored. The remarkable antibacterial, antiviral, and antifungal properties of ginger and its derivatives have been evaluated. Biofilm formation is a common defense mechanism used by microorganisms against antimicrobials. According to a study by Chakotiya et al., ginger inhibits the production of biofilms and disturbs the stability of membranes in Psedomonas aeruginosa, a strain that is resistant to multiple drugs. Excellent antibacterial activity against food-borne pathogenic microorganisms, including Staphylococcus aureus and Escherichia coli, is exhibited by ginger essential oil. Because of some macromolecular components like proteins and nucleic acids, a study revealed that the bactericidal action of ginger essential oil involves destroying cell membrane activity and interfering with energy metabolism. Another study expressed that fresh ginger oil had a moderate antimicrobial effect on Candida, Bacillus subtilis, Trichoderma spp., and Pencillium spp. showed no inhibition, while Aspergillus niger, P. aeruginosa, and Saccharomyces cerevisiae showed a modest effect. It was shown that dried ginger oil exhibited greater antibacterial action against P. aeruginosa. Antioxidant and antibacterial qualities are closely related since inhibiting antioxidant activity may cause antibacterial activity to be retained. Ginger's functional qualities could also be altered during processing and storage, which would alter its antibacterial and antioxidant properties.

iv. Anti-Carcinogenic - Possibility Approximately 10 million of the 19 million cancer cases that were reported globally in 2020 were deadly, making cancer one of the leading causes of death worldwide. Ginger's anticarcinogenic properties against several cancers, including colorectal, prostate, breast, and cervical cancers, have been the subject of much research in recent years. Because chronic inflammation is closely linked to all of the critical phases of cancer formation, it plays a significant role in carcinogenesis. All phases of cancer formation, including start, promotion, advancement, and medication resistance, have been found to be protected against by ginger and its active ingredients. According to an in vitro investigation, a fraction rich in polyphenols from dried ginger powder inhibited the growth of colorectal and stomach adenocarcinoma cells. Studies were conducted both in vitro and in vivo to assess ginger's cytotoxic effects and mode of action against prostate cancer. According to a paper, 6-gingerol, 6-shogaol, 10-gingerol, and 10-shogaol had significant anti-proliferative effects on human prostate cancer cells by deregulating the expression of the proteins GSTπ (glutathione-S-transferase) and MRP1 (multi-drug resistance-associated protein 1). The bifold consolidation of ginger bioactives, such as 6-gingerol, 8-gingerol,

10-gingerol, and 6-shogaol, synergistically reduced the proliferation of PC-3 prostate cancer cells. 6-Gingerol induced human gastric adenocarcinoma (AGS) cells to produce more ROS, which lowers the mitochondrial membrane potential and induces death. 6-shogaol (10–20 μM) was applied in vitro to PC12 cells for 24 hours, improving the phase II antioxidant compounds at the pheochromocytoma cell line in mice and successfully preventing PC12 cells from proliferating under oxidative stress. Conversely, 6-gingerol was unable to shield the PC12 cells from oxidative stress, which may have been caused by the lack of an α, β-unsaturated ketone, a sign of the unit's significance in cytoprotection.

v. **Neuroprotective Activity -** The advent of neurodegenerative disorders, including Parkinson's and Alzheimer's, is possible, and elderly individuals are particularly vulnerable. Ginger may be helpful in the treatment and prevention of neurodegenerative illnesses because of its anti-neuroinflammatory properties and important involvement in memory function, according to numerous recent research. Additionally, 10-gingerol from fresh ginger was revealed to have potent anti-neuroinflammatory properties, as demonstrated by a lipopolysaccharide-activated BV2 microglia culture paradigm. 10. By preventing NF-κB activation, gingerol limited the expression of pro-inflammatory genes, which in turn caused a drop in IL-6, IL-1β, NO, and TNF-α levels. At a 20 μM concentration, ginger-derived phytochemicals, including shogaols and gingerols, have been shown to exhibit potent neuroprotective properties, particularly against Alzheimer's disease. Through many routes, ginger may reduce Aβ-species and cerebral plaques, inhibit cerebral inflammation, modify tau protein, and limit Aβ-induced apoptosis.

vi. **Cardiovascular Protection -** Cardiovascular disease is the leading cause of premature deaths globally, accounting for 17.9 million fatalities annually. Numerous studies have shown that ginger effectively lowers blood pressure and blood cholesterol levels, protecting against cardiovascular illnesses. Mice fed a high-fat diet supplemented with 0.5% lyophilized ginger extract for approximately two weeks showed a decrease in body weight and an increase in serum levels of high-density lipoprotein cholesterol (HDL-C), also referred to as good cholesterol because of its protective properties against cardiovascular diseases.By raising the liver's levels of apoliprotein A-1 and lecithin–cholesterol acyltransferase RNA, ginger extract also promoted the formation of high-density lipoproteins (HDL). Another study confirmed that ginger extract can lower total cholesterol and low-density lipoprotein (LDL). In rats fed a high-fat diet, HDL levels were raised by combining aerobic exercise with a daily oral application of aqueous ginger extract (250 mg/kg of feed) for approximately a month.

vii. **Anti-Obese Activity -** Overweight, or obesity, is a major global concern that results from disruptions in energy metabolism. Adipose (fat) tissues can be divided into two categories based on how they are arranged and behave. While brown adipose tissues are in charge of improving metabolism and energy expenditure, white adipose tissues are mostly used as energy depositories. One innovative strategy to combat obesity is the conversion of white adipose tissues to brown ones. 6-Gingerol may promote cell browning in 3T3-L1 adipocytes through an AMPK-dependent mechanism.In 3T3-L1 preadipocyte cells, gingerenone A was found to exhibit more effective inhibitory activity against adipogenesis and fat formation than gingerol and shogaol. Through the in vivo activation of AMPK, Gingerenone A (50 mg/kg of bodyweight) administered orally daily for 15 weeks also affected the metabolism of fatty acids, impairing diet-induced obesity.

viii. **Anti-Diabetic Effect -** Diabetes mellitus is a long-term metabolic condition marked by insulin resistance and/or insufficiency, which causes blood glucose levels to rise uncontrollably. Advanced glycation end products (AGEs) and protein glycation may be encouraged by chronic hyperglycemia. According to an in vitro investigation, 6-gingerol and 6-shogaol restricted the methylglycoxal (MGO), the precursor of AGEs, to prevent the creation of AGEs and reduced the growth of diabetes complications. Type 2 diabetic mice were given an oral supplement of 6-gingerol (200 mg/kg of corn oil) daily for 28 days. This increased the amount of glycogen stored in the skeletal muscles by stimulating glycogen synthase 1 and improving the presentation of the GLUT4 (glucose transporter type 4) cell membrane[7].

ix.It also posses the following uses.

Anti – bacterial, Anti – fungal, Anti – allergic, Anti – emetic, Hepatoprotective, Bronco protective, Anti – hypertensive, Radioprotective, Flavouring agent[17].

3) Cinnamon

- Synonym : Cinnamomum Zeylanicum
- Biological source: Dried inner bark of genus Cinnamomum
- Family: Lauraceae
- Chemical constituents : Cinnamaldehyde, cinnamic acid, coumarin, catechin, etc. [9]

Uses

i.Diabetes The chronic glucose metabolism condition known as diabetes mellitus is brought on by insulin resistance and beta cell malfunction in the pancreas. Diabetes is a severe medical condition that impacts people of all ages and genders worldwide. Because its physiologically active ingredients increase glucose absorption by triggering insulin receptor kinase activity, insulin receptor autophosphorylation, and glycogen synthase activity, cinnamon has been demonstrated to possess insulin mimetic qualities. In one study, it was shown that a substance called methyl hydroxyl chalcone polymer, which was extracted from cinnamon, increased insulin-dependent glucose metabolism in vitro by about 20 times. By activating the enzyme that causes insulin to bind to cells and inhibiting the enzyme that blocks the process leading to maximal phosphorylation of the insulin receptor, which is linked to increased insulin sensitivity, methyl hydroxyl chalcone polymer, according to Safdar et al., made fat cells more responsive to insulin. A 12-week dose of 500 mg/d of cinnamon, which is high in polyphenolic components, was found to improve impaired fasting glucose and reduce oxidative stress. Another study found that taking 500 mg/d of a particular aqueous extract of cinnamon (Cinnulin PF) for 12 weeks significantly improved several metabolic syndromes, including body composition, systolic blood pressure, and fasting blood sugar. Since metabolic syndrome and cardiovascular disease are related, these findings can have a significant impact on public health.

ii.Anticholesterol - Cinnamon's constituents have been demonstrated to improve blood lipid profiles, insulin control, and glucose absorption. Patients with type 2 diabetes who consumed cinnamon were the subject of a study. The findings demonstrated that individuals who took 1 g, 3 g, or 5 g of cinnamon for 40 days experienced significant reductions in fasting serum glucose (18–29%), triglycerides (23–30%), total cholesterol (12–26%), and low-density lipoprotein cholesterol (7–27%).

iii.Antioxidant - Cinnamon contains polyphenols, which are natural dietary antioxidants that have been demonstrated to inhibit 5-lipoxygenase and so lower oxidative stress in a dose-dependent way. Cinnamon contains a number of specific antioxidant phytochemicals, including epicatechin, camphene, eugenol, gamma-terpinene, phenol, salicylic acid, and tannins. Natural antioxidants are receiving a lot of attention these days, and attempts are being made to replace synthetic ones. Furthermore, the body can avoid oxidative damage by incorporating these natural antioxidants into functional diets.

iv.Cancer - Effective anticancer medicines have been extracted from plants, and 60% of anticancer medications on the market today come from natural sources such microbes, plants, and marine life. Herbs with anticancer qualities have been the subject of several investigations and have been employed as powerful anticancer medications. Cinnamon's anticancer properties have recently been demonstrated to stop the growth of a number of human cancer cell lines, including lung, ovarian, breast, and leukemia tumor cells. It is commonly known that cell adhesion, invasion, and migration are all involved in metastasis, one of the main causes of cancer-related death. One study looked at how CE affected the migration of SiHa (human cervical carcinoma) cells. According to the results, cinnamon considerably decreased the migration of cancer cells, suggesting that it could be used as an anticancer medication to treat cervical cancer. By depolarizing the mitochondrial membrane potential and causing cellular death, CE, which mostly consists of cinnamon aldehyde and a combination of polyphenols, has a therapeutic effect on cervical cancer cells. It was demonstrated in a different study that CE inhibits the proliferation of hematologic malignancy cells. Furthermore, Cox-2 and HIF-1α expression in the tumor tissues, which facilitate cinnamon's strong

anticancer action, decreased when CE was applied to melanoma cell lines. It is widely established that Cox-2 and HIF-1α act as master regulators to exacerbate angiogenesis and metastasis in the course of cancer. Research on effective anticancer medications supports the use of herbal medicine. However, a lot of study and stringent standards for toxicity, safety, quality control, standardization, and clinical trials are needed before using herbal medicine as an anticancer therapy.

v. **Angiogenesis inhibitor -** Angiogenesis is the process by which tumors create new blood vessels in order to encourage growth and spread. One of the most important and particular angiogenesis factors is VEGF. Clinical trials are presently reviewing and examining a variety of VEGF suppression strategies.Serious adverse effects include bleeding, gastrointestinal perforation, and hypertension have been demonstrated for anti-VEGF medications already on the market. Because they are safe for human use, there is a revived interest in finding natural anti-VEGF medicines. Consuming a plant-based diet has also been shown to be useful in preventing the development of cancer. Cinnamon is a natural dietary source of anti-VEGF compounds, according to one study. It was shown that cinnamon and its constituents (such as tetrameric procyanidins and type A procyanidin trimer) efficiently suppressed both VEGF signaling and VEGFR2 kinase activity in endothelial cells. CE reduced the many features of angiogenesis, such as the migration and proliferation of endothelial cells and the development of tumor-induced blood vessels in mice. To identify the main factors causing CE's antiangiogenic effect, more investigation is needed. As a naturally occurring VEGFR2 inhibitor, CE may become a standard dietary approach to cancer prevention and therapy.

vi. **Alzheimer's disease** Memory loss, confusion, poor judgment, and a loss of language abilities are some of the signs of Alzheimer's disease (AD), a progressive, neurodegenerative, and irreversible brain ailment. Numerous investigations have demonstrated that the development of AD is significantly influenced by the buildup of soluble oligomeric assemblies of β-amyloid polypeptides, or amyloid-beta (Aβ). Numerous studies have revealed that compounds derived from natural sources can prevent the development of Aβ plaques. According to a study, cinnamon extract (CEppt) stops Aβ from being harmful to neuronal PC12 cells and suppresses the production of harmful Aβ oligomers. Another study found that giving CEppt orally to a model of aggressive AD transgenic mice improved their cognitive behavior and decreased plaques. According to the findings, using natural substances like cinnamon helps prevent the development of harmful oligomeric Aβ species in AD. AD can develop as a result of intracellular tau neurofibrillary tangles and extracellular plaques (like Aβ). Tangles are useful in the course of neurodegeneration and are created later on in relation to amyloid production. Inhibiting cholinesterase function or amyloid plaque development is the goal of the majority of medications used to prevent or treat AD. The creation of novel medications may be significantly influenced by the compounds that can stop tau from aggregating. Tau is a protein with notable polyrich sections that, under normal circumstances, show little to no structure. Proanthocyanidin timer and cinnamon aldehyde in CE were both responsible for the whole cinnamon extract's effective inhibition of human tau aggregation in vitro when the effects of an aqueous extract of cinnamon containing proanthocyanidins on tau aggregation were investigated.

vii. **Antigastric ulcer -** Peptic ulcers, stomach cancer, and chronic gastritis are all largely caused by Helicobacter pylori. Probiotic microorganisms have been utilized to boost the immune system, prevent inflammatory bowel illnesses, lower the risks of mutagenicity and carcinogenicity, and suppress H. pylori and intestinal infections. Bifidobacterium and Lactobacillus acidophilus-containing yogurt can inhibit H. pylori growth in clinically infected patients. Behrad et al. demonstrated that, for both strains tested, cinnamon yogurt had the most potent inhibitory effect on H. pylori growth in vitro when compared to licorice and control yogurt. According to the study, preparations of cinnamon that have historically been used to treat gastrointestinal issues effectively reduce H. pylori with few or no side effects. The issue of antibiotic treatment resistance may be resolved by these formulations' strong anti-H. pylori action. The drug most frequently used to treat

dyspepsia is simethicone. According to a study, using a cinnamon stomachic mixture can reduce dyspepsia symptoms by 70% and works similarly to simethicone. Compared to simethicone, the cinnamon stomachic combo is thought to be safe, effective, and reasonably priced. It can also boost the favorable response by up to 80% when used for a longer period of time.

viii. **Antibacterial, antifungal** - The oil with the greatest potential for bactericidal effects is cinnamon oil. Cinnamon oil has been shown to have antibacterial properties. Individually or in combination with triclosan, gentamicin, or chlorhexidine, it has been shown to effectively inhibit the formation of biofilms, detach existing biofilms, and kill bacteria in biofilms of clinical strains of Staphylococcus epidermidis. Perhaps the fact that bacteria do not become resistant to essential oils is another reason why essential oils are preferable to antibiotics. To fully understand cinnamon's and its constituents' intricate mechanism of action against S. epidermidis biofilms and other clinically significant microorganisms, more research is necessary. One of the primary ingredients in cinnamon oil is cinnamonaldehyde. It has been demonstrated that cinnamon aldehyde depletes the intracellular ATP levels and destroys the cytoplasmic membrane of both Gram-positive and Gram-negative bacteria. The eggs and adults of human head lice, Pediculus humanus capitis, as well as fungi such as yeasts, filamentous molds, and dermatophytes, are inhibited in their proliferation by cinnamonaldehyde. Cinnamon extracts in water and alcohol have also shown antibacterial activity against Helicobacter pylori. Osteophloeum cinnamon The hardwood species known as the "indigenous cinnamon tree," or kaneh (Lauraceae), has strong antifungal properties. Taiwan's natural hardwood forest is home to the endemic C. osmophloeum tree, whose leaves contain essential oils with chemical components identical to those of C. cassia bark oil. Fungal growth was shown to be strongly inhibited by the essential oils contained in C. osmophloeum leaves. When compared to the other constituents, the primary chemical in leaf essential oils, cinnamonaldehyde, exhibited the strongest antifungal properties. Without debarking the trees, people can easily harvest the leaves to acquire a significant amount of natural bioactive essential oils or cinnamon aldehyde; this could eventually lead to the production of fumigants or preservation agents for wood degradation.

ix. **Nematicidal** - People are becoming more concerned about how pesticides affect human health and the environment, as well as how frequent chemical pesticide applications can have unintended consequences for nontarget organisms. Since they break down into harmless compounds and have minimal negative impact on the environment and nontarget creatures, natural alternative sources such plant essential oils have been proposed. In North America and Japan, dead or dying conifers, such pines, are linked to the pine wood worm, Bursaphelenchus xylophilus. The nematicidal properties of four cinnamon oils and two cassia oils were assessed in one study; the findings indicated that they are effective against adult B. xylophilus and could be a suitable option for a natural control agent.The most hazardous chemical against adult B. xylophilus, according to the study, is cinnamonaldehyde, which is followed by (E)-2 methoxy cinnamonaldehyde and (E)-cinnamic acid.

x. **Acaricidal and repellent effect** - One of the main causes of allergies in human homes are house dust mites (Dematophagoides farina, Dematophagoides pteronyssinus), which can lead to symptoms including atopic dermatitis, asthma, perennial rhinitis, and even newborn death syndrome. Mite species control involves the application of chemical techniques or treatment with repellents like DEET and benzyl benzoate. The frequent use of these compounds, however, has led to the emergence of resistance to them and sparked worries about their potential impact on human health. Since the allergen is not derived from living dust mites but rather from their dead bodies or feces, it is more effective to repel rather than kill them. It is preferable to look for natural repellents, including plants that contain a variety of bioactive compounds, to manage house dust mites. Cinnamon's pure essential oil has been evaluated for its ability to repel and kill house dust mites. It has been found to be a very effective material for this specific goal. It may also lessen chemical resistance and negative health consequences[18].

xi. **It also posses the following uses**

Anti bacterial, Anti inflammatory, Anti oxidant, Immune booster, Flavouring agent

4) Honey

- Synonyms : Madhu
- Biological source : It Is a saccharine fluid (From the nectar of flower) deposited in the honey comb by the hive bee, Apismal- Lifera, Apisdorsata and other species of Apis.
- Family : Apidae.[8]
- Chemical constituents : Glucose, fructose, sucrose, dextrin, formic acid.

Uses - Sweetening agent, Anti-inflammatory, Antibacterial, Antimicrobial.

• 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.[9]

Ingredients	Role of ingredients
Brahmi	Active ingredient
Shankapushpi	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

1) Take clean and dry glassware for experiment, before use.
2) Take 100ml of orange juice in water bath. Add Agar-agar, honey and gelatine with stirring. Heating at 70-75°C.
3) Then add ashwagandha powder with continuous stirring to make mixture uniform.
4) After complete homogenization, the mixture is transfer to molds.
5) Cool the mixture at room temperature for 30 min.
6) Then place in the refrigerator for 24 hours.
7) After 24 hours, gummies remove from the molds and stored in closed container, that keep in refrigerator.

Ingredients	F_1	F_2	F_3
BRAHMI	.5g	.0g	.5g
hankhpushpi	.0g	.5g	.0g
Ginger	.5g	.0g	.5g
Cinnamon	.0g	.0g	.5g
Honey	25g	10g	10g
Orange juice	0ml	0ml	0ml
Gelatine	10g	10g	10g
Agar-Agar	5g	5g	5g
diumBenzoate	.1g	.1g	.1g

Evaluation Parameters of gummies

1) **Physical Evaluation:** The gummies can be examined for appearance like Colour, Odour, Texture, Consistency, Taste, Shape, Transparency
2) **Stickiness and Grittiness:** Texture of the medicated jelly in terms of stickiness and grittiness can be determined by mildly rubbing the jelly between fingers.[11]
3) **p^H :**At room temperature, the jellies' pH was measured using a digital pH meter. For this, 50 ml of distilled water should be mixed with 0.5 g of jelly to create a 1% solution, and the pH should be recorded. Both stability and flavour are influenced by the finished jelly's pH, in addition to both.[10]
4) **Stability:** The stability of the formulation was studied for a period of 4 weeks by keeping it at 4^0 C in refregirator.
5) **Solubility test:** Solubility was obtained by adding the solute in a small amount to a fixed volume of solvents like water ethanol ether and 0.1 N HCl during the pre-formulation solubility analysis.
6) **Microbial examination:** The melted gummy base was struck into the sterile Petri dish under aseptic conditions. The plates were incubated at 37^0C for 24 hours and observed for microbial.
7) **Moisture content:** The moister content was determined by drying finely grounded samples (10g) in a hot air oven at 105 ^{0}C until a constant weight was achieved.
8) **Weight variation:** The jellies were removed from the moulds and weighed. The observed data was reported as mean standard

deviation (SD), with the average weight of 10 jellies being used as the reference point.

9) **Syneresis:** It is when the gel contracts after being stored and the water separates from the gel. It is more noticeable in the gels if a low dose of the gelling agent is used. At room temperature (25°C 5°C) and 8°C 1°C, all the jellies were examined for indications of syneresis. Synergistic formulations were rejected and not chosen for additional research.[3]

10) **Dissolution:** The dissolving media (900ml) and USP paddle device used in in-vitro dissolution studies can be 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 preserved by substituting fresh medium. Using a UV spec trophotometer, the sample's drug content can be determined. % drug release can then be computed. Due to the extremely diverse ingredients, polyherbal medication dissolving testing 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.[12]

11) **Disintegration test:** Disintegration tests can be utilised as an alternative to in vitro dissolving studies for polyherbal jellies. Six polyherbal jellies were chosen at random from various recipes to determine the disintegration time. The disintegration medium was 0.1N HCl, and the temperature was held constant at 37 0.5 °C. The du ration of jellies' disintegration was recorded.[12]

12) **Dispersion time test :** dispersion time test was performed using a flask that contained 100ml of purified water at 37^0C. the CGT from each formulation was placed in the flask and constantly stirred. The time it took for it to disperse completely was observed. The standard requires a dispersion time 10-30mins for CGTs.[13]

CONCLUSION

In conclusion, polyherbal gummies incorporating Brahmi and Shankapushpi hold considerable promise as a modern dosage form for promoting cognitive health. Their integration into therapeutic and preventive healthcare strategies could bridge the gap between traditional Ayurvedic wisdom and contemporary pharmaceutical technology. However, comprehensive pharmacological evaluations, clinical validations, and long-term safety studies are essential to establish their role as effective, evidence-based nutraceuticals.

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