

Development And Evaluation of Polyherbal Gummies for Alzheimer's Disease

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Abstract—Alzheimer's disease is a progressive neurodegenerative disorder characterized by memory loss, cognitive impairment, and neuronal degeneration. The present study focuses on the development and evaluation of polyherbal gummies containing six selected medicinal herbs: Ashwagandha, Brahmi, Tulsi, Turmeric, Amla, and Guava. These herbs were selected based on their reported antioxidant, anti-inflammatory, and potential neuroprotective properties. The herbal extracts were prepared using suitable solvents and incorporated into gummy formulations using gelatin, sucrose, citric acid, sodium benzoate, and flavouring agents. Three formulations (F1, F2, and F3) were developed and evaluated for physical appearance, weight variation, moisture content, surface pH, stickiness, texture, acid-base titration, phytochemical constituents, disintegration time, and drug release characteristics. Preliminary phytochemical screening indicated the presence of various bioactive constituents in the selected herbal extracts. The study aimed to develop a convenient, palatable, and patient-friendly herbal dosage form with potential application in Alzheimer's disease management.

Index Terms—Ashwagandha, Brahmi, Tulsi, Turmeric, Amla, Guava, Citric acid, Sodium benzoate and Gelatin.

I. INTRODUCTION OF DISEASE

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that cause memory loss and other cognitive impairments, such as deterioration in language, learning, memory, visual-spatial abilities, reasoning, and behaviour.^[1]

Alzheimer's disease is the main cause of dementia and quickly becoming one of the most expensive, lethal, and burdening disease of this century.^[2]

The cause of Alzheimer's disease remains poorly understood.^[3] There are many environmental and genetic risk factor associated with its development. The strongest genetic risk factor is from an allele of

apolipoprotein E.^[4] Other risk factors include a history of head injury, clinical depression, and high blood pressure.^[5]

The progression of the disease is largely characterized by the accumulation of malformed protein deposits in the cerebral cortex, called amyloid plaques and neuro fibrillary tangles. These misfolded protein aggregates interfere with normal cell function, and over time lead to irreversible degeneration of neurons and loss of synaptic connections in the brain.^[6]

A probable diagnosis is based on the history of the illness and cognitive testing, with medical imaging and blood tests to rule out other possible causes.^[7]

Initial symptoms are often mistaken for normal brain aging. Examination of brain tissue is needed for a definite diagnosis, but this can only take place after death.^[8]

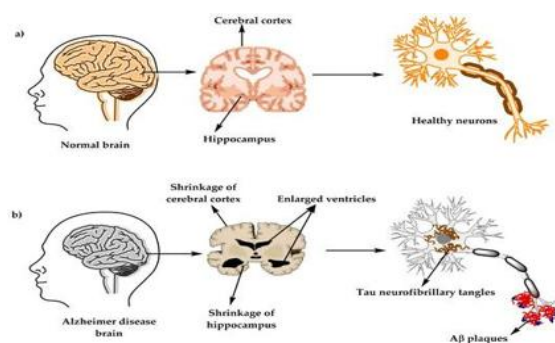


Figure No:1 The physiological structure of the brain and neuron in (a) healthy brain and

(b) Alzheimer's disease (AD) brain.

Alois Alzheimer noticed a presence of amyloid plaques and a massive loss of neurons while examining the brain of his first patient that suffered from memory loss and change of personality before dying and described the condition as a serious disease of the cerebral cortex. Emil Kraepelin named this medical condition Alzheimer's disease for the first time in his

8th edition psychiatry handbook.^[9]

The purpose of this review is to give a brief description about AD diagnosis, pathology, causes, and current treatments, and to highlight the recent development of compounds that could prevent or treat AD by targeting several pathogenic mechanisms, such as A β and tau aggregation, and misfolding, inflammation, oxidative damage, and others. Alzheimer's financial burden on society is large, with an estimated global annual cost of US\$1 trillion.^[10]

Alzheimer's and related dementias are ranked as the seventh leading cause of death worldwide.^[11]

Mckhann et al. noted a significant shift in dementia research in 1976 when Robert Katzman presented data indicating that senile and presenile Alzheimer's disease (AD) were histopathologically identical in older adults (Katzman, 1976). Consequently, the disease garnered increased attention from both the public and the National Institute of Health, which initiated the National Alzheimer's Disease Research Centre Program to investigate the causes, neuropathology, and clinical features of AD.^[12]

Alzheimer's disease or dementia?

Many people wonder what the difference is between Alzheimer's disease and dementia. Dementia is an overall term for a particular group of symptoms. The characteristic symptoms of dementia are difficulties with memory, language, problem-solving and other thinking skill that affect a person's ability to perform everyday activities. Changes to the brain cause dementia, and many different brain changes can lead to dementia. Alzheimer's disease is one cause of dementia. The brain changes of Alzheimer's disease include the excessive accumulation of the protein fragment beta-amyloid and abnormal form of the protein tau, as well as damage to and destruction of neurons. The brain changes of Alzheimer's disease are the most common contributor to dementia. Dementia caused by Alzheimer's disease is called Alzheimer's dementia.

II. ETIOLOGY

Age: Age is the strongest non-modifiable risk factor for Alzheimer's disease (AD). Most cases occur after 65 years of age, with prevalence rising from about 5% in people aged 65–74 to nearly 50% in those older than 85. Aging impairs brain repair mechanisms and increases cardiovascular risk factors, which further

contribute to AD risk. Incidence rises sharply with age, from 2.8 per 1,000 person-years at ages 65–69 to over 56 per 1,000 person-years after age 90.^[13]

Genetics: In sporadic Alzheimer's disease, there is no appearance of a genetic pattern of inheritance. A connection has been found between a gene called Apolipoprotein E (ApoE4) and the development of Alzheimer's diseases. This gene is supposed to be responsible for the protein that carries cholesterol in the blood vessels.^[14]

Education: Lower educational attainment is associated with a higher risk of AD. Higher education may provide a "cognitive or synaptic reserve," allowing the brain to better compensate for neuronal loss during disease progression.^[15]

Coexisting health problems: cardiovascular disease, hypertension, high cholesterol, and type 2 diabetes significantly increase AD risk by impairing cerebral blood flow and metabolism.

As AD progresses, symptoms worsen from mild memory loss to severe cognitive, functional, and behavioral impairments. AD also affects balance and coordination, increasing the risk of falls, injuries, and complications that contribute to mortality.^[16]

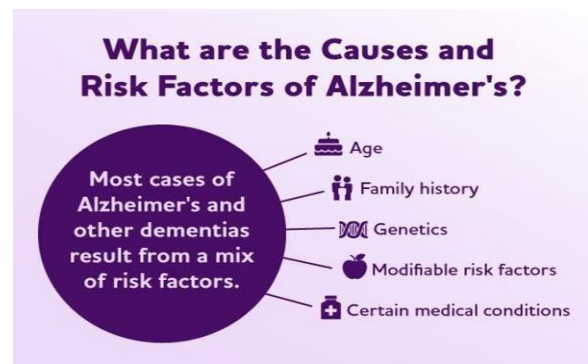


Figure No:2 Causative factors for Alzheimer's disease.

III. SIGNS AND SYMPTOMS

Memory loss and cognitive impairment: Memory loss and cognitive impairment are key indicators of AD. The severity of cognitive impairment correlates best with the burden of neocortical neurofibrillary tangles, which area hallmark of AD.^[17]

Changes in behaviour or personality: Personality changes occur alongside or sometime before cognitive symptoms.^[18] A systematic review showed increased

neuroticism and decreased extraversion, openness, agreeableness and conscientiousness.^[19]

Loss of coordination or balance: Balance and mobility impairments are linearly correlated with cognitive function and can be observed at the beginning of the subjective cognitive decline stage.^[20]

Abnormal gait: Gait parameters can differentiate between healthy elderly, mild cognitive impairment, and AD patients. Gait analysis can potentially contribute to the diagnosis and prognosis of cognitive impairment.^[21]

Loss of sensation or reflexes: loss of sensation may be an indicator of AD. AD patients have a sensory gating deficit, which may result from cholinergic dysfunction and alpha-7 nicotinic receptor loss.^[22]

Abnormal eye movement or vision: Abnormal eye movement or vision can indicate AD. Eye movements, including saccades and smooth pursuit, seem to be slower and less accurate as a result of the disease.^[23]

Tremors or other involuntary movements: Among motor signs during AD, tremor is the least frequent and appears independent of disease progression. As AD progress, the frequency of motor signs like speech/facial expression, rigidity, posture/gait, and bradykinesia also increase.^[24]



Figure No:3 Signs and symptoms of Alzheimer's diseases.

IV. PATHOPHYSIOLOGY

Neuronal loss and or pathology may be seen particularly in the hippocampus, amygdala, entorhinal cortex and the cortical association areas of the frontal, temporal and parietal cortices but also with subcortical nuclei such as the serotonergic dorsal raphe, noradrenergic locus coeruleus and the cholinergic

basal nucleus. The deposition of tangles follows a defined pattern, starting from the trans-entorhinal cortex, the CA1 region of the hippocampus and then the cortical association area, where frontal, parietal and temporal lobes area particularly affected. The extent and placement of tangle formulation correlates well with the severity of dementia, much more so than numbers of amyloid plaques.^[25]

The accretion of tau proteins correlates very closely with cognitive decline and atrophy, including hippocampal atrophy. In the neuropathology of Alzheimer's disease there is a loss and atrophy in temporofrontal cortex, which causes inflammation and deposit the amyloid plaques and an abnormal cluster of protein fragments and tangled bundles of fibers due to this there is an increase in the presence of monocytes and macrophages in cerebral cortex and it is also activates the microglial cells in the parenchyma. Summary of the pathophysiology of Alzheimer's disease are shown in the figure 4.^[26]

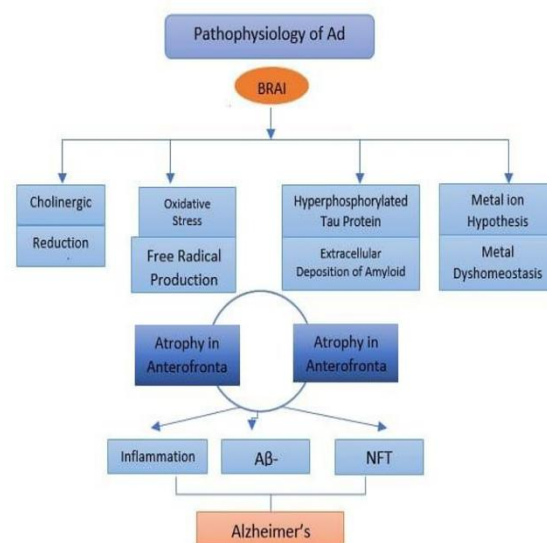


Figure No:4 Hypothesis for pathophysiology of Alzheimer's disease.

V. DIAGNOSIS

Laboratory tests:

Blood tests: Since the discovery of APOE €4 around 25 years ago. Recent research as shown that the Aβ42/40ratio, as determine in the plasma, can distinguish between individuals without cognitive impairment and those with AD. The blood plasma levels of exhibit changes similar to

Cerebrospinal fluid analysis (CSF analysis): According to research, axonal loss and neuronal death cause the intracellular to be released, increasing the tau level in the CSF in AD. CSF T-tau levels are dynamic after acute brain trauma, rising within days after the lesion and remaining high of weeks until returning to normal.^[28]

Those previously documented in cerebrospinal fluid (CSF), suggesting a potential pathway to transit A β between the blood and brain thought the blood-brain barrier (BBB).^[27]

Inflammatory markers:

Noval bio markers:

To identify reliable biomarkers have focused on measuring A β and tau in CSF and blood, as FDG- PET, Pittsburgh compound B-PET, and MRI to measure hippocampal volume.^[29]

Imaging tests:

Computed tomography (CT): is another imaging modality used in Alzheimer's diagnosis, but less frequently the MRI. CT scans provide detailed cross-sectional brain images and can help rule out other pathologies that may mimic AD symptoms. CT scans can reveal structural abnormalities in the brain, such as ventricular enlargement or cortical atrophy, associated with AD.^[30]

Magnetic resonance imaging (MRI): is a non-invasive imaging technique that uses strong magnetic fields to generated detailed brain images. In AD diagnosis, MRI primarily assesses brain structure, detects atrophy, and rules out other potential causes of cognitive impairment, such as tumors or vascular abnormalities. MRI scans reveal brain atrophy, particularly in regions critical for memory formation.^[31]

Positron emission tomography (PET): is a powerful imaging technique that provides functional information about the brain's metabolic and molecular processes. PET scans detect specific hallmarks of AD pathology, such as the accumulation of amyloid plaque and intracellular hyperphosphorylated tau neurofibrillary tangles, as well as changes in glucose metabolism.^[32]

VI. TREATMENT

Cholinesterase inhibitors: Cholinesterase inhibitors function to augment neurotransmission between neuronal synapses to ameliorate Alzheimer's

symptomatology. These pharmacological agents are indicated for individuals with mild to moderate Alzheimer's manifestations.^[33]

Ex: Donepezil, Rivastigmine.

NMDA receptor antagonists in Alzheimer's disease: NMDA receptors play a significant role in AD because they mediate calcium influx and maintain calcium homeostasis in brain. Calcium dysregulation is considered a common mechanism in AD, and hyperactivity of NMDA receptors has been reported in the disease.^[34]

Ex: Memantine, Ketamine.

Antidepressants in Alzheimer's disease: Antidepressant are primarily used to treat mood disorders, recent studies suggest they could also help manage neuropsychiatric symptoms in AD patients, such as depression and agitation.^[35]

Ex: Sertraline, Fluoxetine.

Anxiolytics in Alzheimer's disease: AD is a condition that causes a gradual loss of cognitive abilities. Research has explored the potential neuroprotective effects of N-methyl-D-aspartate for AD. These antagonists are critical for synaptic plasticity and transmission.^[36]

Ex: Trazodone, Buspirone, Hydroxyzine, Gabapentin.

Aducanumab: A monoclonal antibody that approval for treating patients with mild cognitive decline.^[37]

Lecanemab: A monoclonal antibody received approval based on the clarity phase 3 trial, which showed reduction in amyloid plaques burned and cognitive decline.^[38]

Donanemab: Donanemab is a humanized antibody targeting the reduction of amyloid β (A β) plaques in Alzheimer's disease (AD) patients. A randomized clinical trial associated with donanemab, a monoclonal antibody designed, in early symptomatic Alzheimer's disease.^[39]

Ex: Hydroxyzine.

Non pharmacological treatment:

Lifestyle: Lifestyle medicine exploit evidence-based lifestyle interventions in which healthcare practitioners collaborate with patients to evaluated and change various aspects of their lifestyle to avoid, manage, and reverse chronic disease. Several lifestyle changes have

been proven advantageous in AD management, including a healthy diet, regular exercise, good sleep hygiene, socialization and engaging with hobbies, and stress management.^[40]

Future direction in Alzheimer's disease:

Immunotherapy: Active and passive immunization are the two immunotherapeutic approaches which promote amyloid beta and tau clearance.^[41]

Gene therapy: Gene therapy uses different strategies and targets specific regions of the brain in order to treat AD, for example, acting directly on amyloid precursor protein, increase neuroprotection, boosting autophagy-mediated pathways and modulating genes related to lipid metabolism.^[42]

Stem cell therapy: The majority of stem cells used in AD therapy include neural stem cells (NSC) mesenchymal stem (MSC) embryonic stem cell (ESC), and induced pluripotent stem cell (IPSC). Its uses different mechanism in the brain and ultimately can improve cognition.^[43]

Digital therapeutics: Digital therapeutics (DTx) is an emerging field that provides evidence-based therapeutics interventions via internet and software, employing tools such as mobile devices, computer, videogames, apps, sensors, and virtual reality. DTx is used as an adjunctive therapy in AD for improving memory, cognition, functional abilities and managing motor symptoms.^[44]

VII. INTRODUCTION OF POLY HERBAL GUMMIES

Gummies are chewable, gel-based dosage forms that have gained considerable attention in pharmaceutical and nutraceutical fields as an alternative to conventional oral dosage forms. They are designed with an attractive appearance, pleasant taste, and soft texture to improve patient acceptability and ease of administration. Gummies can be formulated using gelling agents such as gelatin, pectin, or gums, along with sweeteners, flavoring agents, Colouring agents, and active pharmaceutical or nutraceutical ingredients. They offer advantages such as convenient administration, no requirement for water during chewing, and improved palatability. Gummies can also be used to incorporate herbal ingredients into a suitable dosage form. However, their formulation requires careful consideration of physical stability,

moisture content, microbial quality, and drug release characteristics.^[45]

History of Medicated Gummies:

Medicated gummies originated from gelatin-based chewy candies developed by the confectionery industry in the early 20th century. Due to their pleasant taste, attractive texture, and ease of consumption, they became widely popular. Recognizing these advantages, the pharmaceutical industry adapted gummies as an alternative oral dosage form for patients who have difficulty swallowing tablets and capsules.

In recent years, medicated gummies have evolved into a novel drug delivery system containing active pharmaceutical ingredients, vitamins, minerals, and herbal extracts. They offer benefits such as improved patient compliance, taste masking, and convenient administration without water. Advantages in formulation technology, including polymer science and flavoring-masking techniques, have enhanced their stability and effectiveness.

Today medicated gummies are widely used in pharmaceutical and nutraceutical applications for both pediatric and adults' population, making them an important and patient-friendly dosage form.^[46]

Advantages of Polyherbal Gummies:

- High consumer acceptability due to pleasant and texture.
- Ease of administration without water.
- Masking of unpleasant herbal flavours through sweeteners and fruits extracts.
- Flexible formulation allowing combination of multiple actives.
- Improved compliances among children and elderly patients.
- Convenient packaging and portability.^[47]

VIII. MATERIALS AND METHODS

Table no 1: Formulation table (F1, F2 and F3)

Ingredients	F1	F2	F3	Uses
Ashwagandha.	0.50	0.25	0.40	Adaptogenic properties and stress reduction
Tulsi	0.20	0.50	0.30	Stress reduction
Brahmi	0.50	0.20	0.40	Memory enhancer and

				neuroprotective agent
Turmeric	0.25	0.50	0.35	Potent antioxidant and anti-amyloid agent
Amla	0.50	0.20	0.35	Oxidative stress, reducing neuroinflammation
Guava	0.20	0.50	0.35	Antioxidant, anti-inflammatory and neuroprotective effect
Galatin	4	4	4	Gelling agent
Sodium benzoate	0.02	0.02	0.02	Preservative
Citric acid	0.20	0.20	0.20	Acidulent
Sucrose	10	10	10	Taste masking agent
Vanilla essence	1-2 drops	1-2 drops	1-2 drops	Flavouring agent
Distilled water	q.s	q.s	q.s	Vehicle

IX. METHODOLOGY

The preparation of gummies involves two separate solution and a sugar solution and a gelling agent solution. In a beaker, 8gm of sucrose was dissolved in 5 to 10 ml of water. The mixture was heated on medium flame with continuous stirring using a glass stirrer. The temperature was carefully controlled to ensure it did not exceed 130°C.

Heating was continued until a viscous sugar syrup was formed. Overheating was avoided to prevent caramelizing of sugars.

Once a thick and uniform syrup was obtained, heating was stopped and the solution was allowed to cool to around 60°C.

In a separated beaker, 4gm of gelatin was mixed with 8ml of water and heated gently on low flame for a few minutes until completely dissolved.

The gelatin solution was then added to the warm sugar syrup and mixed thoroughly. The mixture was reheated briefly to about 70°C to ensure uniform consistency.

The prepared herbal extracts were added to the mixture and stirred well to obtain a uniform dispersion. Add Flavouring agent, citric acid and sodium benzoate were added and mixed properly.

Silicone moulds were lightly lubricated with glycerine to prevent sticking. The warm mixture was poured into the moulds and gently tapped to remove air bubbles and ensure uniform filling.

Any excess material was removed from the moulds.

The filled moulds were kept undisturbed at room temperature for about 60 minutes to allow the gummies to set properly.^[48]



Figure No 5: Preparation of gummies

X. EXTRACTION PROCEDURE OF HERBAL INGREDIENTS

Roots and leaves from Turmeric, Tulsi, Amla, Brhami, Ashwagandha and guava were gathered and sent for verification before proceeding with the extraction. The were roots and leaves cleaned to eliminate contaminants and shade-dried at temperatures between 40–45 °C until they reached a stable weight. The dried roots and leaves were then coarsely ground using a grinder. Exact amounts (50 g) of each powder were extracted individually with a Soxhlet apparatus using 400 mL of methanol or ethanol. The extraction process lasted for about 8 hours, until the solvent in the siphon tube appeared nearly colourless. The resulting extracts were filtered through Whatman filter paper and then concentrated under reduced pressure at 60–70 °C using a heating mantle, resulting in thick methanolic or ethanolic extracts.^[49]



Figure No 6: Powdered drug



Figure No 7: Extraction of Tulsi, Brhami and Turmeric



Figure No 8: Extraction of Ashwagandha, amla and guava

7.3 Phytochemical Screening

Alkaloids Detection Test

Mayer's Test: The extract was combined with Mayer's reagent (a solution of potassium mercuric iodide). The formation of a cream or white precipitate indicated the presence of alkaloids.

Flavonoids Detection Test

Lead Acetate Test: The extract was treated with several drops of lead acetate solution. The presence of a yellow precipitate confirmed the existence of flavonoids.

Tannins Detection Test

Ferric Chloride Test: The extract was treated with 2-3 drops of a 5% ferric chloride solution. The development of a blue, green, or black colour indicated the presence of phenolic compounds.

Saponins Detection Test

Foam Test: The extract was shaken vigorously with distilled water. The presence of a stable foam layer (at least 1 cm high) after 15 minutes indicated the presence of saponins.

Glycosides Detection Test

Keller–Killiani Test: The extract was treated with glacial acetic acid containing a small quantity of ferric chloride, followed by a careful addition of concentrated sulfuric acid. The development of a brown ring at the interface indicated the presence of cardiac glycosides.^[50]

Table no 2: Observations of phytochemical test.

<p>Ashwagandha</p>	
<p>Turmeric</p>	
<p>Tulsi</p>	
<p>Amla</p>	
<p>Brahmi</p>	
<p>Guava</p>	

XI. EVALUATION PARAMETER FOR GUMMIES

The prepared formulations (F1, F2 and F3) were evaluated for physical appearance and various physicochemical parameters such as weight variation, moisture content, surface pH, stickiness test, texture and firmness, acid base titration, drug content uniformity, dissolution, disintegration. All evaluations were performed in duplicate and the results are expressed as mean $\pm$ standard deviation (SD).

- Physical Appearance
- Weight Variation Test
- Moisture Content
- Surface pH
- Stickiness Test
- Acid – Base Titration
- Dissolution Test

Physical appearance:

Organoleptic Characteristics: The prepared gummies were visually and sensorially evaluated for colour, taste, odour, and appearance. The gummies exhibited a uniform green colour, smooth surface and soft chewy texture.

Weight variation test:

The weight variation test is performed to determine the uniformity of weight of the prepared gummies. Select 10 gummies from the prepared batch and weigh each gummy individually using a calibrated analytical balance. Record the individual weights and calculate the average weight by dividing the total weight of all 10 gummies by 10. Then, calculate the percentage weight variation of each gummy using the formula.

Percentage weight variation = $(| \text{Individual weight} - \text{Average weight} | / \text{Average weight}) \times 100$. Compare the obtained results with the specified acceptance criteria to determine the uniformity of weight among the gummies.

Moisture content:

The moisture content of gummies is determined by the loss-on-drying method. Initially, weigh a clean, dry weighing dish and record its weight. Take a known quantity of gummies, place them in the dish, and record the combined weight. Dry the sample in a hot-air oven at 105°C until a constant weight is obtained. After drying, cool the dish in a desiccator and weigh it again. Calculate the moisture content by determining

the difference between the initial and final sample weights and express the result as a percentage using the formula.

Moisture content (%) = $[(\text{Initial sample weight} - \text{Dry sample weight}) / \text{Initial sample weight}] \times 100$.

The obtained value indicates the percentage of moisture present in the gummies. The drying temperature and duration should be validated for the formulation to avoid decomposition or loss of volatile ingredients

Surface pH:

The pH of the gummies was determined by dissolving 2g of gummy in 10 mL of distilled water and measuring with a pH indicator paper at room temperature.

Stickiness Test:

The stickiness of the gummies was assessed manually by gently pressing two gummies together and observing adhesion.

Acid-Base Titration:

The total acidity of the gummy formulation was determined by acid-base titration. 2g sample of gummy was dissolved in 20 mL of distilled water, and the solution was titrated against 0.1 N NaOH using phenolphthalein as an indicator. The endpoint was marked by the appearance of a faint pink colour. The acidity level was calculated and found within acceptable range, ensuring balanced flavour and pH stability.^[51]

Disintegration Test:

The disintegration test is performed to determine the time required for gummies to break down into smaller particles under specified experimental conditions. Take the required number of gummies and place them in container containing the specified medium. Maintain the temperature and other conditions according to the selected test method. Observe the gummies at regular intervals and record the time required for them to break down. Note any remaining residue and record the observations. The disintegration time of the gummy formulation is then determined and reported.

Dissolution Test:

Place the required volume of suitable dissolution medium in the dissolution apparatus and maintain the

temperature at $37 \pm 0.5^\circ\text{C}$. Add the gummy to the vessel and operate the apparatus at the specified rotation speed. Withdraw samples at predetermined time intervals and replace them with an equal volume of fresh medium. Filter the samples and analyze the drug concentration using UV-visible spectrophotometry. Calculate and record the percentage of drug released at each time interval.^[52]

XII. RESULTS

Table No 3: Phytochemical evaluation of Guava and Ashwagandha extracts.

Sl no	Chemical constituents	Tests	Guava	Ashwagandha
1	Alkaloids	Mayers test	Absent	Present
2	Flavonoids	Lead acetate test	Present	Present
3	Tannins	Ferric chloride test	Present	Present
4	Saponins	Foam test	Present	Present
5	Glycosides	Killer-Killian test	Absent	Absent

Table No 4: Phytochemical evaluation of Tulsi and Brahmi extracts.

Sl no	Chemical constituents	Tests	Tulsi	Brahmi
1	Alkaloids	Mayers test	Present	Absent
2	Flavonoids	Lead acetate test	Present	Present
3	Tannins	Ferric chloride test	Present	Present
4	Saponins	Foam test	Present	Present
5	Glycosides	Killer-Killian test	Absent	Present

Table No 5: Phytochemical evaluation of Turmeric and Amla extracts.

Sl no	Chemical constituents	Tests	Turmeric	Amla
1	Alkaloids	Mayers test	Absent	Present
2	Flavonoids	Lead acetate test	Present	Present
3	Tannins	Ferric chloride test	Present	Present
4	Saponins	Foam test	Absent	Present
5	Glycosides	Killer-Killian test	Absent	Absent

XIII. EVALUATION PARAMETER FOR GUMMIES

Physical Appearance

Organoleptic characteristics

The formulated gummies were green, had a pleasant flavour, a smooth glossy surface and were soft cohesive, indicating good formulation uniformity.

Weight variation test

Average weight-2.0g per gummy

Range- 1.52-2.2g

Within acceptable pharmacopoeia limits ($\pm 5\%$)

Moisture content:

The moisture content of the prepared polyherbal gummies was found to be F1 8%, F2 6.5% and F3 7% indicating acceptable moisture level and good stability of the formulation

Stickiness Test

A mild surface was observed when two gummies were pressed together.

Surface pH

The pH of the gummy solution was found to be F1 4.8, F2 5.0 and F3 4.9 which falls within the acceptable range for oral formulations, ensuring flavour stability and product safety.



Figure No 9:



pH Test

Acid-Base titration

Titration at a 2g gummy solution with 0.1N NaOH using phenolphthalein indicator showed the end point at F1 10.5, F2 11.9 and F3 15.5



Figure No 10: sample



Figure No 11: Acid Base Titration

Disintegration Test:

The disintegration test was performed on the gummy formulation under specified experimental conditions. The gummies were observed at regular intervals to determine the time required for them to break down into smaller particles. The disintegration time was recorded, F1 15mins, F2 14mins and F3 18mins.

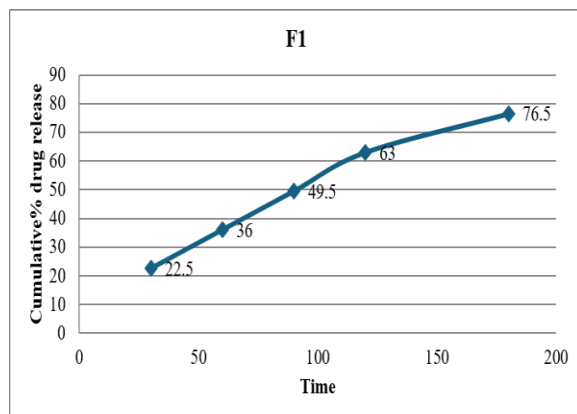


Figure No 12: Disintegration Test

Dissolution Test

Table No 7: F1 Graph representation

Time	Absorbance	Concentration	Amount Released	% drug released
30 min	0.25	24mg/ml	22.5mg	22.5%
60 min	0.40	40mg/ml	36mg	36%
90 min	0.55	55mg/ml	49.5mg	49.5%
120 min	0.70	70mg/ml	63mg	63%
180 min	0.85	85mg/ml	76.5mg	76.5%

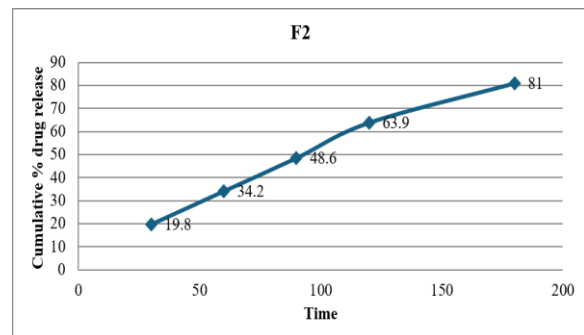


X axis = Time

Y axis= Cumulative% Drug Release

Table No 8: F2 Graph representation

Time	Absorbance	Concentration	Amount Released	% drug released
30 min	0.22	22mg/ml	19.8mg	19.8%
60 min	0.38	38mg/ml	34mg	34%
90 min	0.54	54mg/ml	48.6mg	48.6%
120 min	0.71	71mg/ml	63.9mg	63.9%
180 min	0.90	90mg/ml	81.0mg	81%

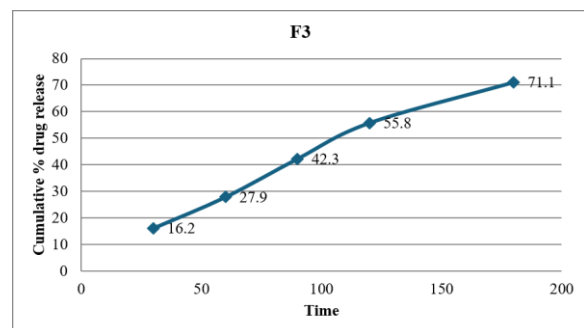


X axis = Time

Y axis= Cumulative% Drug Release

Table No 9: F3 Graph representation

Time	Absorbance	Concentration	Amount Released	% drug released
30 min	0.18	18mg/ml	16.2mg	16.2%
60 min	0.31	31mg/ml	27.9mg	27.9%
90 min	0.47	47mg/ml	42.3mg	42.3%
120 min	0.62	62mg/ml	55.8mg	55.8%
180 min	0.79	79mg/ml	71.1mg	71.1%



X axis = Time

Y axis= Cumulative% Drug Release

Table no 10: Evaluation of Polyherbal Gummies

Parameters	F1	F2	F3
Colour	Light Greenish	Smooth Greenish	Dark Greenish
Odour	Herbal odour	Herbal odour	Herbal odour
Texture	Smooth	Smooth	Smooth
Chewiness	Easily chewable	Easily chewable	Easily chewable
Weight Variation	2-3 g	2-4 g	1-3 g
pH	4.8	5.0	4.9
Acid Base Titration	10.5	11.9	15.5
Stickiness	Non sticky	Non sticky	Non sticky
Moisture Content	1.84	1.87	1.89
Disintegration	15 minutes	14 minutes	18 minutes
Dissolution	76.5	81	71.1



Figure No 14: Prepared gummies

XIV. DISCUSSION

The present study was undertaken to develop and evaluate a polyherbal gummy formulation intended to provide a convenient herbal dosage form with potential neuroprotective benefits in Alzheimer's disease. The selected herbal extracts were incorporated into a gummy base containing suitable gelling, sweetening, flavouring and other excipients. The gummy dosage form was selected because it is easy to administer, palatable, portable and may improve patient acceptability and compliance, particularly in individuals who have difficulty swallowing conventional tablets or capsules.

Phytochemical screening was performed to identify the major classes of phytochemicals present in the selected herbal ingredients. The results showed the presence of different phytochemical constituents, including flavonoids, tannins, saponins, alkaloids, and glycosides, depending on the herbal material tested. Flavonoids and tannins were detected in most of the selected herbs, while the presence of alkaloids, saponins, and glycosides varied among the samples. The prepared polyherbal gummies were evaluated for appearance, colour, odour, taste, texture, weight variation, thickness, pH, moisture content, drug/extract content and other relevant physical parameters. Weight variation testing was carried out to assess the uniformity of the prepared gummies. This evaluation is important because consistent weight helps maintain uniformity between individual units of a formulation. The moisture content of the formulations was also evaluated to understand the amount of moisture retained in the prepared gummies. The recorded moisture content was 8% for F1, 6.5% for F2, and 7% for F3. Among the three formulations, F2 showed the lowest recorded moisture content. The surface pH of the prepared gummies was evaluated to determine their acidic nature. The recorded pH values were 4.8 for F1, 5.0 for F2, and 4.9 for F3. These results indicated that all three formulations had similar, mildly acidic pH values.

The disintegration test was performed to determine the time required for the gummies to break down under the specified test conditions. The recorded disintegration times were 15 minutes for F1, 14 minutes for F2, and 18 minutes for F3. Among the three formulations, F2 showed the shortest disintegration time, followed by F1 and F3. This result indicated that F2 disintegrated more rapidly than the other formulations under the conditions used in the study. An in-vitro dissolution study was conducted to evaluate the drug release pattern of the formulated gummies over time. The percentage of drug released increased with time in both formulations. For F1, drug release increased from 22.5% at 30 minutes to 76.5% at 180 minutes, whereas F2 showed an increase from 19.8% at 30 minutes to 81% at 180 minutes. Among the two formulations, F2 exhibited the highest drug release (81%) at 180 minutes, indicating a better drug release profile under the experimental conditions. Thus, based on the recorded final dissolution values, F2 demonstrated comparatively better overall in-vitro release

performance. The formulation showed acceptable physical characteristics, indicating that the selected excipients and manufacturing process were suitable for producing a stable and elegant gummy dosage form.

XV. CONCLUSION

Development and evaluating polyherbal gummies for Alzheimer's disease using selected herbal extracts of Ashwagandha, Tulsi, Brahmi, Turmeric, Amla and Guava. The selected herbs possess reported antioxidant, anti-inflammatory, neuroprotective and cognitive-supporting properties, making them suitable candidates for incorporation into a polyherbal formulation. The herbal extracts were successfully prepared and subjected to preliminary phytochemical screening. The extracts showed the presence of various phytoconstituents, particularly flavonoids, tannins, saponins, alkaloids and glycosides, depending on the individual extract. These phytoconstituents may contribute to the reported antioxidant and neuroprotective potential of the selected herbs. Three formulations, F1, F2 and F3, were successfully prepared using gelatin as the gelling agent along with sucrose, citric acid, sodium benzoate and flavouring agent. The prepared gummies showed satisfactory organoleptic characteristics, including smooth texture, acceptable appearance, herbal odour and easy chewability. The formulations were further evaluated for weight variation, pH, moisture content, stickiness, acid-base titration, disintegration and dissolution.

Among the prepared formulations, F2 showed comparatively better overall performance, with a pH of 5.0. Considering the overall evaluation results, F2 appeared to be the most promising formulation among F1, F2, and F3 because it showed the shortest disintegration time of 14 minutes, the lowest recorded moisture content of 6.5%, and the highest reported curcumin release of 81% at 180 minutes. These findings suggest that F2 had comparatively favourable characteristics among the formulations evaluated in the present study. Nevertheless, the final selection should also consider the accuracy and consistency of the recorded weight variation, moisture content, and dissolution data. The progressive drug release observed during the dissolution study indicates that the gummy formulation can provide release of the incorporated herbal constituents over the tested period.

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