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FORMULATION AND EVALUATION OF GARLIC ENTERIC COATED TABLET FOR NEURODEGENERATIVE DISEASE

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ABSTRACT

Garlic belongs to the Alliaceae family and has been known and used for centuries for medicinal purposes. Its sulfur compounds, enzymes, amino acids, and minerals contribute to its antibacterial, antifungal, antiviral, and antioxidant properties. This herb has been used as a prevention agent against cardiovascular diseases, cancer, and neurodegenerative diseases. The chemistry of garlic occurs by the conversion of alliin to allicin, which is responsible for its medicinal property. Extracts from garlic show inhibitory effects on various kinds of microorganisms such as bacteria, fungi, and viruses. Preparation of Tablets Various Methods Used in Tablet Manufacture: Wet Granulation, Dry Granulation, Direct Compression. Excipients Tablet Formulation: Diluents, Binders, Glidants, Lubricants, Disintegrating agents, Colouring agents and antiadherents. Neurodegenerative diseases are a type of disease characterized by progressive neuronal loss in the central nervous system, for example, Alzheimer's and Parkinson's diseases. Neuroprotective effects have been attributed to garlic, which could help in preventing or treating such diseases.

KEYWORDS: Alliaceae, Neuroprotective, Colouring, antiadherents.

1. INTRODUCTION

Garlic, *Allium sativum L.* is a member of the Alliaceae family, has been widely recognized as a precious spice and a popular remedy for diverse illnesses and physiological problems. The term garlic may also have originated from the Celtic word 'all' which means smelly. Cultivated all around the world, garlic seems to have originated in critical Asia and then unfold to China, the close to East, and the Mediterranean vicinity earlier than shifting west to critical and Southern Europe, Northern Africa (Egypt) and Mexico. Garlic has been used for heaps of years for medicinal purposes.

Sanskrit records display its medicinal use about 5000 years in the past, and it has been used for as a minimum 3,000 years in Chinese medicine. The Egyptians, Babylonians, Greeks, and Romans used garlic for its medicinal activities.[1]

Pasteur discovered garlic's antibacterial properties in 1858, and it was utilized as an antiseptic to prevent gangrene during World Wars I and II. Garlic is being used to prevent and treat cardiovascular disease by decreasing blood pressure and cholesterol, as an antibiotic, and as a cancer prevention agent. Several complex sulfur-containing chemicals that are quickly absorbed, altered, and metabolized constitute the active ingredients. Data from many randomized studies show that garlic reduces overall cholesterol levels by around 10% and improves HDL/LDL ratios. Garlic is also beneficial as a moderate antihypertensive, lowering blood pressure by 5-7% in randomized studies. Garlic also reduces clots on injured endothelium by inhibiting platelet aggregation and increasing fibrinolytic activity. In vitro results imply antibacterial activities; however, they have not been tested in human trials.[2]

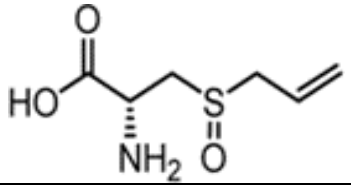
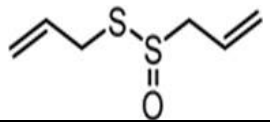
CHEMISTRY OF GARLIC

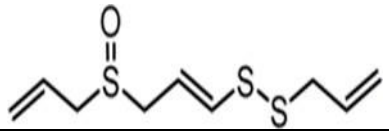
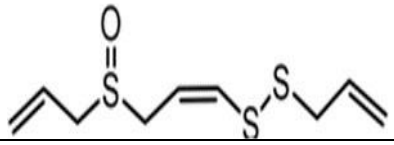
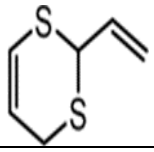
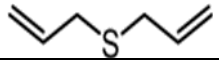
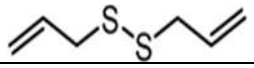
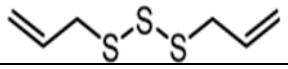
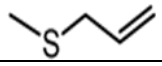
Garlic consists of at the least 33 sulfur compounds, several enzymes, 17 amino acids, and minerals together with selenium. It incorporates a better concentration of sulfur compounds than any other Allium species. The sulfur compounds are accountable both for garlic's smelly scent and many of its medicinal outcomes. Dried, powdered garlic contains about 1% alliin (S- allyl cysteine sulfoxide). Allicin (diallyl thiosulfinate or diallyl disulfide), one of the most physiologically active substances, is not present in garlic until it is crushed or chopped; damage to the garlic bulb releases the enzyme allinase, which converts alliin to allicin. Vinyldithiines are produced by further metabolism of allicin. At room temperature, this breakdown takes place in hours, and when cooking, it happens in minutes. Since it was first chemically isolated in the 1940s, allicin has been used to combat a wide range of bacteria, fungi, viruses, and parasites.

None of the garlic preparations—garlic oil, aged garlic, and steam-distilled garlic—appears to have as much physiologic activity as fresh garlic or garlic powder; instead, they contain different byproducts of the transformation of allicin rather than significant amounts of alliin or allicin.[3]

Numerous phytochemicals, including sulfur-containing compounds (Table 1), have been found in A. sativum bulbs. These compounds include ajoenes (E-ajoene, Z-ajoene), thiosulfinates (allicin), vinyldithiins (2-vinyl-(4H) -1,3-dithiin, 3-vinyl-(4H)-1,2-dithiin), sulfides (diallyl disulfide (DADS), diallyl trisulfide (DATS), and others. Together, these compounds account for 82% of the sulfur content in garlic.[4]

Table 1: List and structures of some of the sulfur-containing compounds isolated from *Allium sativum*.[5]

Compounds	Molecular formula	Structure
Alliin	$C_6H_{11}NO_3S$	
Allicin	$C_6H_{10}OS_2$	

E-Ajoene	$C_9H_{14}OS_3$	
Z-Ajoene	$C_9H_{14}OS_3$	
2-Vinyl-4H-1,3-dithiin	$C_6H_8S_2$	
Diallyl sulfide (DAS)	C6H10S	
Diallyl disulfide (DADS)	C6H10S2	
Diallyl trisulfide (DATS)	C6H10S3	
Allyl methyl sulfide (AMS)	C4H8S	

Pharmacological Activities of Garlic and Its Related Compounds Antibacterial Activity

Garlic is known for its antimicrobial properties, which are ascribed to its allicin content. This compound has been observed to exhibit antimicrobial activity against a diverse range of microorganisms, encompassing both Gram-positive and Gram-negative bacteria that are resistant to antibiotics, as well as bacteria like Shigella, Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, Streptococcus mutans, Salmonella enterica, Klebsiella aerogenes, Vibrio, Mycobacteria, Proteus vulgaris, and Enterococcus faecalis. A number of pathogenic bacteria have been shown to be inhibited in their development by various garlic extracts (aqueous, chloroform, methanolic, and ethanolic extracts), with variable degrees of sensitivity.[6]

Garlic extracts also inhibited the growth of other harmful intestinal bacteria including enterotoxigenic E. Coli strains, which are the primary cause of diarrhea in both people and animals. Garlic has been shown to have antibacterial properties as well as the ability to stop bacterial infections from producing toxins. Additionally, allicin shown efficacy against methicillin-resistant S. aureus (MRSA). Because it oxidizes protein cysteine or glutathione residues under physiological circumstances, allicin interacts chemically with thiol-containing enzymes such as RNA polymerase, alcohol dehydrogenase, and thioredoxin reductase to provide antimicrobial activity. Because all living cells include thiol groups, allicin is a dose- related biocide that can affect cysteine proteinase's vital metabolism and destroy all eukaryotic cells.[7]

Antifungal Activity

Garlic extracts demonstrated a broad-spectrum fungicidal activity against a variety of fungus, including species of Candida, Torulopsis, Trichophyton, Aspergillus, Trichosporon, and Rhodotorula, It was recently shown that garlic extract inhibits the germination and proliferation of Rhodotorula mucilaginosa and Meyerozyma guilliermondii.[8]

Allicin and garlic oil had strong antifungal properties, against A. Niger and Candida albicans. These effects were achieved by entering both the cellular membrane and the membranes of organelles, such as the mitochondria, which resulted in the destruction of organelles and cell death.[9]

Antiviral Activity

The antiviral interest of garlic extracts has been evaluated towards influenza B, human rhinovirus kind 2, human cytomegalovirus (HCMV), Parainfluenza virus type 3, herpes simplex type 1 and a couple of, vaccinia virus, and vesicular stomatitis virus.[10] Allicin functions by inhibiting several thiol enzymes, whereas ajoene's antiviral properties stem from its ability to stop leukocyte fusion and adhesive contact. Diallyl trisulfide proved successful in inhibiting HCMV replication and early viral gene expression. It works by boosting the activity of natural killer cells (NK cells), which eliminate virus-infected cells.[11]

Antioxidant Activities

According to a recent paper, eating garlic often increases endogenous antioxidant synthesis or lowers the generation of oxidizers such oxygen-free radical species (ORS), which in turn boosts internal antioxidant activities and minimizes oxidative unfavourable effects. The antibiotic gentamycin has been used to treat a variety of bacterial infections. It has been shown to decrease plasma albumin levels and increase the enzymes aspartate transaminase and alanine aminotransferase, both of which are known to cause liver damage. Garlic has been shown to mitigate hepatotoxicity caused by acetaminophen and gentamycin by enhancing antioxidant status and controlling oxidative stress.[6] ROS is at the core of many ailments, it is justified to assume that the antioxidant effect of garlic might be through modulation of ROS, increasing glutathione and cellular antioxidant enzymes. Moreover, garlic extract was found to increase the activities of some antioxidant enzymes (e.g., superoxide dismutase (SOD)) and decrease glutathione peroxidase (GSH-Px) in hepatic tissues of rats. Notably, several reports indicated that AGE rich in flavonoid, phenol, and different sulfur compounds.[12]

Anticancer Activity

Raw garlic extract was found to be the most effective and highly specific anticancer drug when compared with 33 raw vegetable extracts against different cancer cells without affecting the non-cancerous cells. The anticancer mechanisms of garlic extracts were attributed to the inhibition of cell growth and proliferation, regulation of carcinogen metabolism, stimulation of apoptosis, prevention of angiogenesis, invasion, and migration and thus reducing the anticancer agent’s negative effects. Interestingly, in 1960, tumor cells were reported to be killed when incubated in an allicin solution. Allicin isolated from garlic was reported to suppress colorectal cancer metastasis through enhancing the immune function and preventing the formation of tumor vessels as well as survivin gene expression to enhance the cancer cell’s apoptosis. It also can enhance the treatment of pancreatic cancer thereby invert gene silencing and restrain cancer cell proliferation. Recent research revealed that allicin can prevent gastrointestinal cancer cells MGC 803 proliferation and induce apoptosis, which can be accomplished through enhancing p38 expression. Allicin-derived polysulfanes have been reported to target microtubules, which lead to interruption of the cell- cycle and finally to apoptosis. Several studies reported the activity of allicin in preventing cell proliferation by targeting tubulin that shapes the mitotic spindle and thus inhibits cell division.[13]

Activities Related to Metabolic Diseases Effect on Diabetes Mellitus

Ethanolic garlic extracts exhibited an antidiabetic effect against streptozotocin- and alloxan-induced diabetic mice and rabbits by activating the insulin secretion from parietal cells of the pancreas. Another clinical study examined the antidiabetic effect of garlic pills administration at 900 mg/day in patients with type II diabetes and hyperlipidemia and they reported that garlic pills decrease the cholesterol, serum lipids, and fasting blood sugar. Moreover, allyl propyl disulfide, allicin, cysteine sulfoxide, and S-allyl cysteine sulfoxide decreased the blood glucose level by preventing the insulin activation caused by liver, enhancing the secretion of insulin from pancreatic beta cells, isolation of insulin from the bonded forms, and increasing the cell sensitivity to insulin.[14]

Effect on obesity

Overweight and obesity are defined as abnormal or excessive fat accumulation that presents a risk to health. Body fat distribution is important because abdominal obesity, rather than other fat depots, is strongly associated to metabolic syndrome (MetS), together with hypertension, atherogenic dyslipidemia, hyperglycemia, and prothrombotic and proinflammatory conditions.[15] Worldwide rise of obesity is a result of complex interactions between genetic factors and obesogenic environments, garlic is one of the most important vegetables with bioactive properties, including its by-products. Evidence from in vitro, animal, and human research has shown that garlic or its sulfur-containing compounds have beneficial effects on obesity and MetS. Allicin was shown to potentially prevent obesity and associated metabolic disorders by enhancing the expression of brown adipocyte-specific genes, including UCP-1, through KLF15 signal cascade.[16]

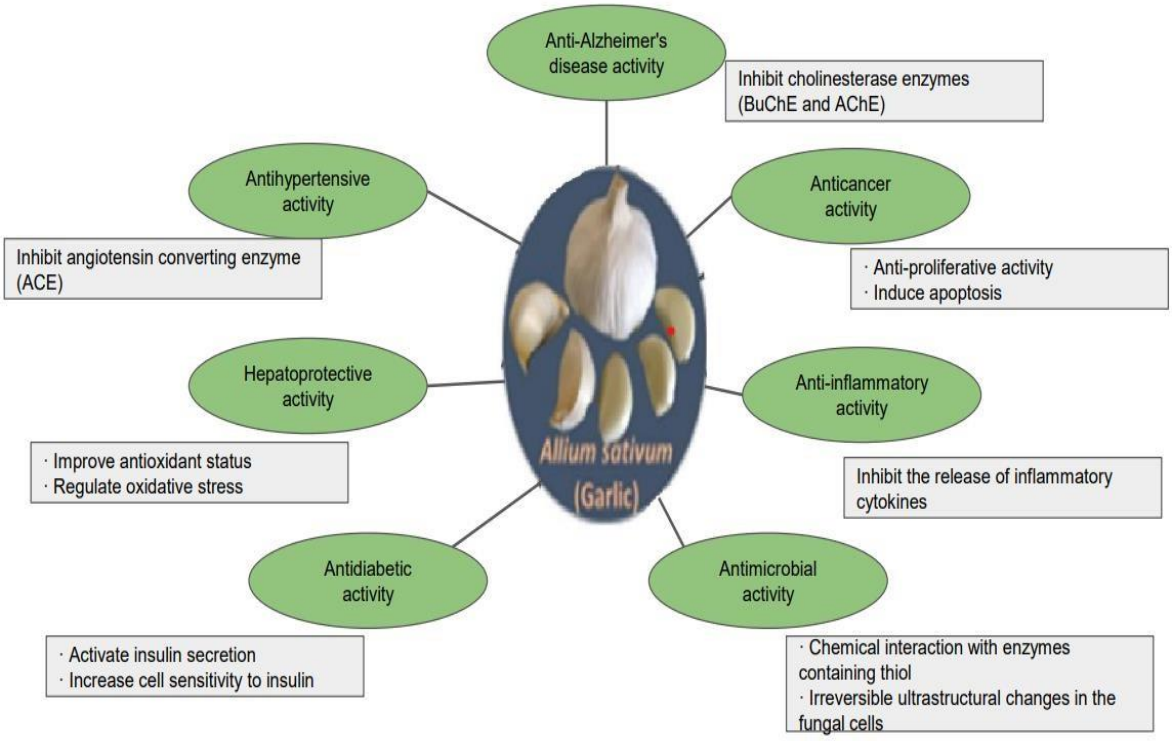


Figure 1: Different pharmacological activities of garlic (*Allium sativum*) and their mechanisms.

Table 2: The pharmacological activity of garlic (*Allium sativum*) and its related compounds.[5]

Activities	Bioactive Compound	Mechanism of Action
Antibacterial	Allicin	Chemical interaction with enzymes containing thiol.
Antifungal	DADS	Irreversible ultrastructural changes in the fungal cells, loss of structural integrity and affected the germination ability.
	DATS	
Antiviral	Allicin	Chemical interaction with enzymes containing thiol.
	DATS	Enhancing Natural killer-cell (NK-cell) activity that destroys virus-infected cells.
Antiprotozoal	Allicin	Preventing the parasite's RNA, DNA and protein synthesis.
	DATS	
	Ajoene	Inhibiting the human glutathione reductase and T. cruzi trypanothione reductase.
Antioxidant	Allicin, DADS, and DATS	Modulation of ROS, increasing glutathione and cellular antioxidant enzymes.
	Alliin	Controlling ROS generation and preventing mitogen-activated protein kinase (MAPK).
	DAS	Suppressing the enzymatic activity of cytochrome P450-2E1, reducing the generation of reactive oxygen and nitrogen species.
Anti-inflammatory	Allicin	Enhancing the immune cell activity f, inhibiting the SOFla chemokine and Transendothelial migration of neutrophils.
	DAS	Diminishing the expression of the inflammatory cytokines (e.g., NF- KB, IL- 1ß, and TNF-a), and ROS generation by suppressing CYP-2E1 hepatic enzyme.
	Thiacremonone	Blocking the NF-kB activity.
Anti-cancer	Allicin, allin, DADS, DAS	Enhancing p38 expression.
	Z-Ajoene	Stimulating apoptosis in human leukemic cells, promoting the peroxide production, caspase-3-like, and caspase-8 activities.
Immunomodulatory	Allicin	Suppressing BuChE and AChE.
Anti-obesity	Ajoene	Decreasing the fat accumulation in 313-1.1 adipocytes and dramatically decreases the body weight gain.
	1,2-Vinyldithiin	Decreasing the C/EBPa, PPARy2, and LPL expression and the PPARy effect in human adipocytes.
Antidiabetic	Allyl propyl disulfide, allcin,	Decreasing the insulin secretion from pancreatic cells, increasing
	cysteine sulfoxide S-allyl cysteine sulfoxide, allin	liver metabolism, and thus and enhancing the short-acting insulin production.
Hypolipidemic, hypocholesterolaemic	Different garlic preparations	Decreasing serum IC, TG, and LDL levels and moderately elevating HDL cholesterol.
Anti-Atherosclerotic, antithrombotic	Different garlic preparations	Preventing ADP-activated platelets binding to immobilized fibrinogen and platelet aggregation, inhibiting GPU by Ila receptor and increasing cAMP.
Antihypertensive	Gamma- glutamylcysteine	Inhibiting the angiotensin-converting enzyme.

TABLET

According to the Indian Pharmacopoeia pharmaceutical tablets are solid, flat or biconvex dishes, unit dosage form, prepared by compressing a drug or a mixture of drugs, with or without diluents. Tablet is defined as a compressed solid dosage form containing medicaments with or without excipients. They vary in shape and differ in size and weight, depending on number of medicinal substances and the intended mode of administration.

Properties

- Should be an elegant product having its own identity while being free of defects such as chips, cracks, discoloration and contamination.
- Should have strength to withstand the shocks encountered in its production, packaging, shipping and dispensing.

- Should have the physical stability to maintain its physical attributes over time.
- Must be able to release the medicament agent in the body in a predictable and reproducible nature.
- Must have a suitable chemical stability over time.[17]

Different types of tablets

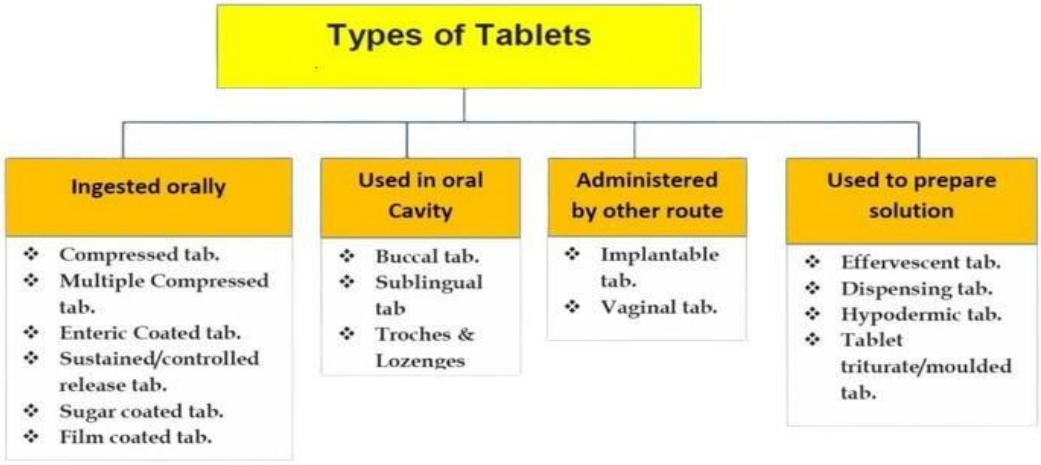


Figure 2: Different types of tablets.

TABLET MANUFACTUTING METHODS

Dry granulation

The dry granulation process is used to form granules without using a liquid solution. This type of process is recommended for products, which are sensitive to moister and heat. Forming granules without moisture requires compacting and densifying the powders. Dry granulation can be done on a tablet press using slugging tooling. On large-scale roller compactor commonly referred to as a chilsonator. The compacted mass is called slugs, and the process is known as slugging. The slugs are then screened or milled to produce a granular form of tablet materials, which have the good flow properties then original powder mixture. The main advantage of dry granulation is it requires less equipment and eliminates the addition of moisture and the application of heat, as found in wet massing and drying steps of the wet granulation method. The manufacture of oral solid dosage forms such as tablets is a complex multi-stage process under which the starting materials change their physical characteristics a number of times before the final dosage form is produced. Traditionally, tablets have been made by granulation, a process that imparts two primary requisites to formulate: compatibility and fluidity. Both wet granulation and dry granulation (slugging and roll compaction) are used. Regardless of whether tablets are made by direct compression or granulation, the first step, milling and mixing, is the same; subsequent step differ. Numerous unit processes are involved in making tablets, including particle size reduction and sizing, blending, granulation, drying, compaction, and (frequently) coating. Various factors associated with these processes can seriously affect content uniformity, bioavailability, or stability.

Wet granulation

This is the most widely used method of tablet preparation. In this method the powders are bound by suitable binder by “adhesion”. The binder is added by diluting with suitable solvent prior to addition to the blended powders to form wet granules which in turn are dried suitably to expel the solvent forming dried granules. The surface tension forces, and capillary pressure are primarily responsible for initial granules formation. The main advantage being it meets all the requirements for tablet formation though it is multistage, time consuming.

Directly compression

The tablets are made by directly compressing the powdered materials without modifying the physical nature of the materials itself. Direct compression is done for the crystalline materials having good physical properties such as flow property, compressibility. Main advantages of direct compression are time saving, safety of operations and low cost.[18]

Advantages of direct compression

- Direct compression is economic compared to wet granulation since it requires fewer unit operations. This means less equipment, lower power consumption, less space, less time, and less labour leading to reduced production cost of tablets.
- More suitable for moisture and heat sensitive APIs, since it eliminates wetting and drying steps and increases the stability of active ingredients by reducing detrimental effects.
- The high compaction pressure involved in the production of tablets by slugging or roller compaction can be avoided by adopting direct compression.
- Changes in dissolution profiles are less likely to occur in tablets made by direct compression on storage than in those made from granulations. This is extremely important because the official compendium now requires dissolution specifications in most solid dosage forms.
- Disintegration or dissolution is the rate-limiting step in absorption in the case of tablets of poorly soluble API prepared by wet granulation. The tablets prepared by direct compression disintegrate into API particles instead of granules that directly come into contact with dissolution.
- The chances of wear and tear of punches and dies are less.[19,20]

Table 3: Ideal requirements, advantages, and limitations of direct compression.

Ideal requirement	Advantage	Limitation
Flowability	Cost effective production	Segregation
Compressibility	Better stability of API	Variation in functionality
Dilution potential	Faster dissolution	Low dilution potential
Rework ability	Less wear and tear of punches	Rework ability
Stability	Simplified validation	Poor compressibility of API
Controlled particle size	Lower microbial contamination	Lubricant sensitivity

Factors in formulation development

Many factors influence the choice of the optimum direct-compression filler to be used in a tablet formulation. More than in any other type of tablets, successful formulations of direct compression tablets depend on careful consideration of excipient properties and optimization of the compressibility, fluidity, and lubricability of powder blends. The importance of standardizing the functional properties of the component raw materials and the blending parameters cannot be overstressed. Preformulation studies are essential in direct compression tableting even for what would appear to be a simple formulation.[21]

Excipients Used for Tablet Formulation

Pharmaceutical excipients are the substances other than the active drug, used in pharmaceutical dosage forms. The excipients are considered as inert substances, they do not have any active role in therapeutics, but they can be used to support the process to produce an effective product. Different types of excipients used in tablet manufacturing are:

1. Diluents

Diluents are fillers used to make required bulk of the tablet when the drug dosage itself is inadequate to produce the bulk. Secondary reason is to provide better tablet properties such as improve cohesion, to permit use of direct compression manufacturing or to promote flow. Example: Lactose, Spray dried lactose, Micro crystalline cellulose

2. Binders

Binders are used as binding agent in tablets; it provides cohesive strength to powdered materials. Binders are added in both dry and wet form to form granules. Example: Gelatin, glucose, Lactose, cellulose derivatives-Methyl cellulose, Ethyl cellulose, Hydroxy propyl methyl cellulose, Hydroxy propyl cellulose, starch.

3. Glidants

These are improving the flow of powders during tablet manufacturing by reducing friction and adhesion between particles. Also used as anti-caking agents. Example: Colloidal anhydrous silicon and other silica compounds

4. Lubricants

Used to reduce the friction between die wall and tablet, prevent adhesion of tablet to dies and punches. Helps in easy ejection of tablets from die cavity. Classified into 2 types. Example: Insoluble- Stearic acid, Magnesium stearate, Calcium stearate, Talc, Paraffin. Soluble- Sodium lauryl sulphate, Sodium benzoate, PEG 400, 600,8000 etc.

5. Disintegrating agents

Disintegrating agents are the substances that are added to an oral solid dosage form such as tablets, beads, pellets, granules as well as capsules to promote its rapid disintegration or break down into small particles after administration for facilitating rapid dissolution into GI fluid. Example: Starch, Cellulose derivatives, and alginates, Crospovidone.

6. Colouring agents

Improve acceptability to patients, aid identification and prevent counterfeiting. Increase stability of light-sensitive drugs. Synthetic dyes and natural colours. Compounds that are themselves natural pigments of food may also be used.

7. Anti-adherents

These are added to prevent adhesion of tablet material to punches and dies.

Example: Talc

8. Flavouring agents

Flavouring agent means a therapeutically inert, nonallergenic substance consisting of inactive ingredients that is added to a drug to improve the drug's taste and palatability. Example: volatile oil (anise oil), aldehyde (vanillin), ginger oil, peppermint oil, and lemongrass oil.

9. Sweetening agent

Sweetening agent are substances that sweeten and mask the taste of food, beverages, and medications to make them palatable to the consumer. Example: Glucose, Dextrose, Fructose, Mannitol, Maltose, sorbitol.[22]

TABLET COATING

Tablet coating is a process in pharmaceutical manufacturing that involves the application of a thin layer of coating material onto the surface of tablet cores. The coating material is applied to provide various benefits such as protection, improved appearance, taste masking, controlled release, or targeted drug delivery. Tablet coating can be performed using different techniques, including sugar coating, film coating, enteric coating, or other specialized coating methods.

Techniques of Tablet Coating

1. Sugar coating
2. Film coating
3. Enteric coating

1. Sugar Coating

Sugar coating is one of the oldest and most traditional methods of tablet coating. It involves the application of multiple layers of sugar-based coatings to the tablet core. The sugar coating provides a visually appealing appearance and masks the taste and odour of the tablet. The process of sugar coating typically includes several steps such as sealing, sub coating, smoothing, colouring, and polishing. This coating technique is time-consuming and labour- intensive, but it offers protection to the tablet from environmental factors and provides an elegant, finished product.

2. Film Coating

Film coating is a widely used method in tablet coating due to its efficiency and cost- effectiveness. It involves the application of a thin polymer film onto the tablet surface. The polymer film is typically composed of cellulose derivatives such as hydroxypropyl methylcellulose (HPMC) or ethyl cellulose. Film coating provides a smooth, glossy, and uniform appearance to the tablet while protecting it from environmental factors, such as moisture and light. Film coatings can also incorporate additional functionalities such as delayed release or taste masking.

3. Enteric Coating

Enteric coating is a specialized type of tablet coating designed to protect the tablet from gastric acid and deliver the active ingredient to the intestines. This coating is resistant to the acidic environment of the stomach but dissolves in the more alkaline conditions of the small intestine. Enteric coating is typically composed of polymers such as cellulose acetate phthalate (CAP) or hydroxypropyl methylcellulose phthalate (HPMCP). It is used for drugs that are sensitive to gastric acid or that need to be released in a specific region of the gastrointestinal tract. Enteric-coated tablets are commonly used to prevent gastric irritation or to ensure the targeted delivery of drugs.[23]

Polymers used for enteric coating are as follow:

- Cellulose acetate phthalate (CAP)
- Acrylate polymers
- Hydroxy propyl methyl cellulose phthalate
- Polyvinyl acetate phthalate[24]

Advantages of Enteric Coating

- Protect the drug from the stomach.
- Protect the acid liable drugs from the gastric fluid e. g. enzymes and certain antibiotics.

- Coatings are necessary for tablets that have an unpleasant taste, and a smoother finish makes large tablets easier to swallow.
- Forbid gastric distress or nausea due to irritation from a drug, e.g., sodium salicylate.
- Deliver drugs intended for local action in the intestines, e. g. intestinal antiseptics could be delivered to their site of action in a concentrated form.[25]

Neurodegenerative diseases

Neurodegenerative diseases (NDDs) are a heterogeneous group of neurological disorders adversely affecting the lives of millions of people worldwide and entail the progressive loss of neurons in the central nervous system (CNS) or peripheral nervous system (PNS). The collapse of the structure and function of neural networks and loss of neurons, which are unable to efficiently renew themselves due to their terminally differentiated nature, result in the breakdown of the core communicative circuitry, culminating in impaired memory, cognition, behaviour, sensory, and/or motoric function.[26]

During childhood, neural stem cells produce many neurons, the number of which is significantly reduced in adulthood. Although neurons are not immortal, the progressive loss of neurons, neuron structure, and/or their functions, known as neurodegeneration, is central to the pathophysiology of several brain disorders and is also a major health concern. Neurodegeneration is associated with dysfunction of the synapse, neural network, and the deposition of physiochemically altered variants of proteins in the brain. Diseases with neurodegeneration as their hallmark feature are collectively termed as Neurodegenerative disease.[27]

The most common NDs include Alzheimer's disease, Parkinson's disease, prion disease, Amyotrophic lateral sclerosis, motor neuron disease, Huntington's disease, spinal muscular atrophy, and spinocerebellar ataxia.

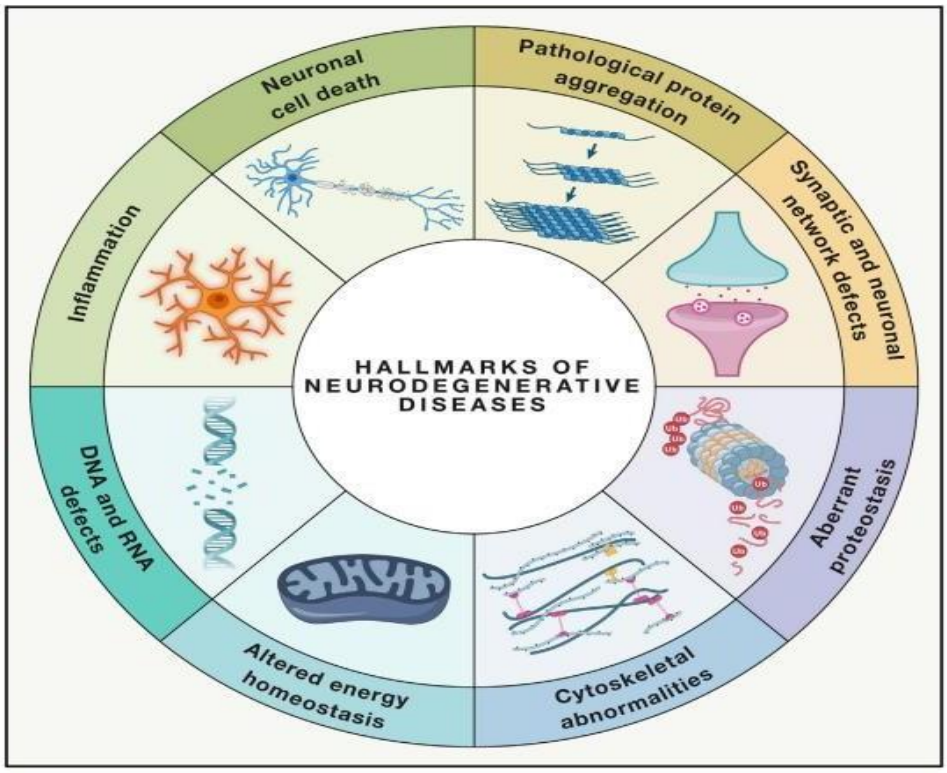


Figure 3: Hallmarks of neurodegenerative diseases.

ALZHEIMER'S DISEASE

Alzheimer's disease (AD) is a progressive, neurodegenerative brain disorder that slowly destroys memory, thinking, and reasoning skills. It is the most common cause of dementia, affecting millions of people worldwide, primarily older adults but also younger individuals in rare cases.

Causes and Pathology

The exact cause of AD remains elusive, but several factors are believed to play a role:

- **Amyloid plaques:** These are abnormal clumps of a protein called beta-amyloid that build up between brain cells.
- **Tau tangles:** These are twisted fibers of another protein called tau that accumulate inside brain cells.
- **Inflammation:** Chronic inflammation in the brain may contribute to cell damage and death.
- **Genetics:** While not deterministic, some gene variations increase the risk of developing AD.[28]

Symptoms and Progression

AD symptoms typically worsen gradually over time, often starting with mild memory problems:

- **Early stage:** Difficulty remembering recent events, names, or where things are placed. Losing track of thoughts or conversations. Misplacing belongings frequently.
- **Middle stage:** More significant memory loss, forgetting close family and friends. Difficulty with problem-solving, planning, and speaking clearly. Confusion, disorientation, and personality changes.
- **Late stage:** Complete dependence on others for basic needs. Inability to communicate, walk, or respond to surroundings.[29]

Stages of Alzheimer's Disease

- **Preclinical:** No symptoms, but brain changes have begun.
- **Mild cognitive impairment (MCI):** Noticeable memory decline, but daily life remains manageable.
- **Dementia due to AD:** Symptoms significantly impact daily life and require assistance.
- **Severe dementia:** Total dependence on others, loss of speech and motor skills.[30]

Diagnosis and Treatment

There is no cure for AD, but diagnosis can help manage symptoms and slow progression. Doctors use cognitive tests, brain scans, and blood tests to rule out other causes.

Treatment aims to:

- **Manage symptoms:** Medications like cholinesterase inhibitors and memantine can help with memory, thinking, and behaviour.
- **Support cognitive function:** Activities like puzzles, socialization, and physical exercise can stimulate the brain.
- **Address behavioural changes:** Therapies can help manage anxiety, aggression, and sleep disturbances.[31]

PARKINSON'S DISEASE

Parkinson's disease (PD) is an age-related disorder that is characterized by degeneration of dopaminergic neurons in substantia nigra pars compacta (SNpc) Substantia nigra is located within the midbrain and contains two main sections: pars compacta and pars reticulata. Over 80 % of the dopaminergic neurons are in SNpc and these neurons are the primary source of dopamine.[32]

Causes and Pathology

While the exact cause of Parkinson's disease (PD) remains elusive, scientists have identified several key factors that contribute to its development:

1. Loss of Dopamine-Producing Neurons

- The primary culprit is the degeneration and death of dopamine-producing neurons in the substantia nigra, a part of the midbrain responsible for controlling movement.
- This loss of dopamine disrupts the delicate balance of chemicals in the brain, particularly the basal ganglia, a circuit that controls movement initiation and coordination.

2. Alpha-Synuclein and Lewy 7 odies

- A protein called alpha-synuclein abnormally clumps together inside nerve cells, forming Lewy bodies, a hallmark of PD pathology.
- The exact role of alpha-synuclein and Lewy bodies in cell death is still being researched, but they are thought to disrupt essential cellular processes and trigger inflammation.

3. Genetic and Environmental Factors

- Genetic mutations**:** Certain gene variations, like those in the PARKIN gene, increase the risk of PD, though most cases are not purely genetic.
- Environmental factors**:** Exposure to toxins like pesticides or head injuries might play a role, but the evidence is not conclusive.[33]

Pathological Processes

- **Mitochondrial dysfunction:** Mitochondria, the "powerhouses" of cells, are often impaired in PD neurons. This can lead to energy depletion and contribute to cell death.
- **Oxidative stress:** An imbalance of free radicals and antioxidants damages cells and contributes to neurodegeneration.
- **Inflammation:** Chronic inflammation in the brain can contribute to cell injury and death.

Additional factors

- **Age:** PD typically affects older adults, with the risk increasing with age.
- **Sex:** Men are slightly more likely to develop PD than women.

Research hope

- **Gene therapy:** Replacing faulty genes or introducing healthy ones to prevent or slow cell death.
- **Stem cell therapy:** Transplanting healthy dopamine-producing cells into the brain to replace lost ones.
- **Neuroprotective drugs:** Protecting existing dopamine neurons from degeneration.[34]

2. LITERATURE REVIEW

Imaizumi et al. (2023) conducted a systematic review and meta-analysis of 22 randomized controlled trials investigating the effects of garlic intake on cardiovascular risk factors. Their findings revealed significant reductions in total cholesterol, low-density lipoprotein cholesterol (LDL-c), and triglycerides, suggesting a potential role for garlic in

managing cardiovascular diseases. This is particularly relevant for neurodegenerative diseases, as vascular dysfunction is considered a key contributing factor in their pathogenesis.

Moein et al. (2023) reviewed the medicinal and therapeutic properties of garlic, garlic essential oil, and garlic-based snack foods. They highlighted the antioxidant, antiviral, and anti- inflammatory properties of these products, which are known to play a crucial role in preventing or delaying the progression of neurodegenerative diseases.

Bhuiyan et al. (2023) investigated the neuroprotective effects of garlic extract against beta- amyloid-induced neurotoxicity in an in vitro model of Alzheimer's disease. Their study demonstrated that garlic extract effectively protected neurons from oxidative stress and apoptosis, suggesting its potential for preventing neuronal damage in Alzheimer's disease.

Ahmed et al. (2022) evaluated the efficacy of enteric-coated garlic tablets in improving cognitive function in a rat model of Alzheimer's disease. They observed significant improvements in memory and learning in treated animals compared to controls, suggesting the potential of enteric-coated garlic tablets for managing cognitive decline in Alzheimer's disease patients.

Khan et al. (2022) assessed the effects of enteric-coated garlic tablets on neuroinflammation in a mouse model of Parkinson's disease. Their findings revealed a decrease in pro- inflammatory markers and improved motor function in treated animals, highlighting the potential of enteric-coated garlic tablets for reducing neuroinflammation and improving motor symptoms in Parkinson's disease.

Ziaei et al. (2022) evaluated the effects of garlic tablets on plasma lipids and platelet aggregation in pregnant women at high risk of preeclampsia. Their findings suggested that garlic tablets may have beneficial effects on cardiovascular health, which could be indirectly beneficial for reducing the risk of neurodegenerative diseases.

Ademiluyi et al. (2022) investigated the modulatory effects of dietary garlic on gentamycin- induced hepatotoxicity and oxidative stress in rats. Their study demonstrated the hepatoprotective and antioxidant properties of garlic, suggesting its potential for improving liver function and reducing oxidative stress, which are also relevant to neurodegenerative diseases.

Aydin et al. (2022) reviewed the current literature on the role of garlic in neurodegenerative diseases. They highlighted the potential mechanisms of action through which garlic may exert its neuroprotective effects, including antioxidant, anti-inflammatory, and anti-apoptotic activities.

Ahangar-Sirous et al., (2022) age-related Neurological Disorders (ANDs) involve neurodegenerative diseases (NDDs), such as Alzheimer's Disease (AD), the most frequent kind of dementia in elderly people, and Parkinson's Disease (PD), and also other disorders like epilepsy and migraine. Although ANDs are multifactorial, aging is a principal risk factor for them. The common and most main pathologic features among ANDs are inflammation, oxidative stress, and misfolded proteins accumulation. Since failing brains caused by ANDs impose a notable burden on public health and their incidence is increasing, a lot of works have been conducted to overcome them. Garlic, *Allium sativum*, has been used for different medical purposes globally and more than thousands of publications have reported its health benefits. Garlic and aged garlic extract are considered potent anti-inflammatory and antioxidants agents and

can have remarkable neuroprotective effects. This review is aimed to summarize knowledge on the pharmacotherapeutic potential of garlic and its components in ANDs.

Liu et al. (2021) conducted a meta-analysis of 10 randomized controlled trials investigating the effects of garlic supplementation on cognitive function in individuals with mild cognitive impairment. Their findings revealed significant improvements in memory and global cognitive function in the garlic group compared to the control group, suggesting potential benefits for delaying cognitive decline in mild cognitive impairment patients.

Higuera-Valenzuela et al. (2020) analyzed the neuroprotective effects of aged garlic extract against beta-amyloid-induced neurotoxicity in a mouse model of Alzheimer's disease. They observed significant reductions in amyloid plaque formation and cognitive impairments, highlighting the potential of aged garlic extract for neuroprotection.

Rezaei et al. (2018) evaluated the effects of garlic powder supplementation on motor function and neuroinflammation in a rat model of Parkinson's disease. Their results demonstrated significant improvements in motor performance and reductions in pro-inflammatory markers, suggesting the potential of garlic for managing Parkinson's disease symptoms.

El-Ansary et al. (2017) investigated the anti-neurodegenerative effects of garlic extract in a Drosophila model of Alzheimer's disease. They observed significant improvements in lifespan, memory, and motor function in treated flies, suggesting potential neuroprotective effects mediated by antioxidant and anti-inflammatory pathways.

B.C. Mathew et al., (2016) Garlic has been investigated extensively for health benefits. It is considered one of the best disease preventive foods, based on its potent and varied effects. Garlic is best known for its lipid lowering and anti-atherogenic effects. Mechanisms of action include inhibition of the hepatic activities of lipogenic and cholesterogenic enzymes that are thought to be the genesis for dyslipidemias, increased excretion of cholesterol and suppression of LDL-oxidation. Oxidative stress caused by increased accumulation of reactive oxygen species (ROS) in cells has been implicated in the pathophysiology of several neurodegenerative diseases including Alzheimer's disease (AD). Several studies have demonstrated the antioxidant properties of garlic and its different preparations including Aged Garlic Extract (AGE). AGE and S-allyl-cysteines (SAC), a bioactive and bioavailable component in garlic preparations have been shown in a number of in vitro studies to protect neuronal cells against beta-amyloid toxicity and apoptosis. Thus, the broad range of anti- atherogenic, antioxidant and anti-apoptotic protection afforded by garlic may be extended to its neuroprotective action, helping to reduce the risk of dementia, including vascular dementia and AD.

Adaki, Shridevi; et al., (**2014**) Garlic is one of the components, which have effects on reducing the risk of cancer. Including garlic in the diet helps for the betterment of the health. Recently, studies were carried out to know its effect on the cancer cell lines. Many studies have shown its effects not only on carcinomas, but also on the cardiovascular system and immune system. Functions of each component of the garlic were studied to know exactly, which component has beneficial effect.

Leyla Bayan, et al., (**2014**) recent studies support the effects of garlic and its extracts in a wide range of applications. These studies raised the possibility of revival of garlic therapeutic values in different diseases. Different compounds in garlic are thought to reduce the risk for cardiovascular diseases, have anti-tumor and anti-microbial effects, and show benefit on high blood glucose concentration. However, the exact mechanism of all ingredients and their long- term

effects are not fully understood. Further studies are needed to elucidate the pathophysiological mechanisms of action of garlic as well as its efficacy and safety in treatment of various diseases.

Chia-Wen Tsai et al., (**2012**) garlic one of the best-researched herbal remedies, holds a unique position in history, traditionally employed to treat infection, colds, diabetes, heart disease, and a host of other disorders. Clinically, it has been evaluated for lowering blood pressure, cholesterol, and glucose concentration, as well as for the prevention of arteriosclerosis and cancer. Epidemiologically, garlic consumption inversely correlates with the risk of oral, stomach, esophageal, colon, and prostate cancers. In addition, the biological activities of garlic, including antibacterial, antithrombotic, antioxidant, immunomodulatory, and antidiabetic actions and modulation of drug metabolism, have been extensively investigated. Here, we briefly summarize the recent findings on garlic and its sulfur-containing compounds in preventing cardiovascular diseases and cancer, along with its modulation of drug- metabolizing enzymes and membrane transporter activities.

S. V. Rana et al., (**2011**) the present article reviews the historical and popular uses of garlic, its antioxidant, haematological, antimicrobial, hepatoprotective and antineoplastic properties and its potential toxicity (from sulfoxide). Garlic has been suggested to affect several cardiovascular risk factors. It has also been shown that garlic and its organic allyl sulfur components are effective inhibitors of the cancer process. Since garlic and its constituents can suppress carcinogen formation, bioactivation and tumour proliferation, it is imperative that biomarkers be established to identify which individuals might benefit most. Garlic powder, aged garlic and garlic oil have demonstrated antiplatelet and anticoagulant effects by interfering with cyclo-oxygenase-mediated thromboxane synthesis. Garlic has also been found to have synergistic effects against *Helicobacter pylori* with a proton pump inhibitor. The active compound allicin may affect atherosclerosis not only by acting as an antioxidant, but also by other mechanisms, such as lipoprotein modification and inhibition of LDL uptake and degradation by macrophages. Freshly prepared garlic homogenate protects against isoniazid+rifampicin-induced liver injury in experimental animal models. Several mechanisms are likely to account for this protection.

Londhe V.P et al., (2011) The active constituents are sulfur containing compounds that are rapidly absorbed and metabolized. Numerous studies suggest that garlic lowers total cholesterol concentrations by approximately 10%, favorably altering HDL/LDL ratios. Literature survey support garlic's effectiveness as a mild antihypertensive, lowering blood pressure by 5-7%. Garlic inhibits platelet aggregation and enhances fibrinolytic activity, reducing clots on damaged endothelium. Another important use of garlic is as antidiabetic. Garlic controls the blood sugar level by different types of mechanisms. In vitro studies and animal data suggest that garlic may help to prevent some solid tumors. Therefore, garlic is also effective in the cancer prevention. There are no studies evaluating its effectiveness in treating children or pregnant or nursing women. The other proposed uses of garlic include the hepatoprotective, anthelmintics, anti-inflammatory, antioxidant, antifungal and wound healing.

Farhath khanum et al., (**2010**) epidemiological as well as laboratory studies have shown that garlic consumption reduces certain cancer incidences in the stomach, colon, mammary, cervical, etc. Garlic has been shown to metabolized into N-acetyl-S-allyl cysteine, allyl mercaptan, diallyl disulfide, diallyl sulfide, diallyl sulfoxide, diallyl sulfone, and allyl methyl sulfide. Garlic has been thought to bring about its anticarcinogenic effect through a number of mechanisms, such as the scavenging of radicals, increasing gluathione levels, increasing the activities of enzymes such as glutathione S-transferase, catalase, inhibition of cytochrome p4502E1, DNA repair mechanisms, prevention of

chromosomal damage etc. Future research should standardize the dosage of garlic and type, i.e., whether it should be taken fresh, cooked, or aged.

Małgorzata Iciek, et al., (2009) garlic enhances immune functions and has antibacterial, antifungal and antivirus activities. It is known to prevent platelet aggregation, and to have hypotensive and cholesterol- and triglyceride-lowering properties, although the latter features have been questioned. This review is focused on anticancer efficacy of *Allium sativum and* attempts to explain the mechanisms of this action. Medicinal properties of garlic rely upon organosulfur compounds mostly derived from alliin. Organosulfur compounds originating from garlic inhibit carcinogen activation, boost phase 2 detoxifying processes, cause cell cycle arrest mostly in G2/M phase, stimulate the mitochondrial apoptotic pathway, increase acetylation of histones. Garlic-derived sulfur compounds influence also gap-junctional intercellular communication and participate in the development of multidrug resistance.

Dinesh Kumar Singh **et al.,** (**2008**) garlic (Allium sativum L.), is a valuable spice plant used as a food item as well as medicine in different parts of the world. Researchers from various disciplines are now directing their efforts towards discovering the effects of garlic on human health. Interest among the researchers particularly those in the health profession, has stemmed from the search for a drug that has a broad-spectrum therapeutic effect with minimal toxicity. Recent researches indicate that garlic extract has antimicrobial activity against many genera of bacteria, fungi and virus. Garlics role in preventing cardiovascular disease has been acclaimed by several research groups. Chemical constituents of garlic have been investigated for effect on hyperlipidemia, hypertension, platelet aggregation and blood fibrinolytic activity. Experimental data on animals and some epidemiological studies clearly indicate that garlic may provide protection against cancer. This possibility needs to be fully explored. Recent research in field of pest control indicate that garlic preparation has strong insecticidal, nematicidal, rodenticidal and molluscicidal activity. Although field trials and laboratory experiments on the pesticidal activity of garlic has been conducted, yet the more research are recommended to study the exact mode of action, way of delivery in environment for effective control of pest.

3. AIM AND OBJECTIVES

Aim

The primary goal of our research is to develop a pharmaceutical formulation of garlic in the form of an enteric-coated tablet specifically designed for the treatment and potential management of neurodegenerative diseases.

Objectives

1. To formulate garlic enteric coated tablets using different concentration of excipients.
2. To evaluate the physicochemical properties of the formulated garlic enteric coated tablets, including tablet appearance, hardness, friability, uniformity of weight, content uniformity, and dissolution characteristics.
3. To evaluate the in vitro release profile of the garlic tablet, which will help us understand how the tablet dissolves and releases its active ingredients.
4. To optimize the formulation of the garlic tablet to ensure that it is pharmaceutically stable, cost-effective, and of high quality.

The rationale for selecting neurodegenerative disease

Neurodegenerative diseases like Alzheimer's, Parkinson's, and Amyotrophic lateral sclerosis (ALS) are affecting a rapidly growing population, causing immense personal and societal suffering. Estimates suggest around one billion

people globally are affected by neurological disorders, for example, Alzheimer's disease alone affects an estimated 50 million people worldwide. Nearly 10 million new cases of dementia, a common symptom of many neurodegenerative diseases, are diagnosed each year as per the World Health Organization. Currently, there are no cures and limited effective treatments for most neurodegenerative diseases. Enhancing the existing treatments would have a profound impact on the lives of patients and their families.

Reason for choosing enteric coating for Garlic

The reason we chose enteric coating for garlic is that it helps to protect the active ingredients in garlic from being destroyed by stomach acid. Garlic contains a compound called allicin, which is responsible for its many health benefits, including its potential to help with neurodegenerative diseases. However, allicin is unstable and can be easily destroyed by stomach acid. By using enteric coating, we can ensure that the garlic tablet reaches the small intestine before it dissolves, where it can be absorbed into the bloodstream and exert its beneficial effects. Enteric coating also helps to prevent the garlic tablet from causing bad breath or other digestive issues.

4. PLAN OF WORK

1. Standard curve of Garlic

- Determination of λ_{max} of Garlic
- Preparation of calibration curve of Garlic

2. Compatibility studies

- Fourier transform Infrared spectroscopic studies to determine the interaction between drug and excipients.

3. Pre-compression parameters

- Bulk density
- Tapped density
- Carr’s index
- Haussner’s ratio
- Angle of repose

4. Formulation of core tablets, by direct compression

5. Post compression parameters

- Weight variation
- Hardness
- Thickness
- Friability
- Drug content determination
- Disintegration time
- In-vitro dissolution studies

5. PLANT AND EXCIPIENTS PROFILES

1. GARLIC

Figure 4: *Allium Sativum L.* plant.

1. Botanical Information

Botanical name: *Allium sativum L*

Synonyms: Garlic

Family: Amaryllidaceae

2. Vernacular Names

English: Garlic

Tamil: Poondu

Hindi: Lahsun

Malayalam: Veluthulli

Telugu: Vellulli

3. Classification

Kingdom: Plantae

Clade: Tracheophytes

Clade: Angiosperms

Clade: Monocots

Order: Asparagales

Family: Amaryllidaceae
Subfamily: Allioideae
Genus: Allium
Subgenus: A. subg. Allium
Species: A. sativum[35]

4. Description

Allium sativum is a herbaceous, perennial plant producing 6 - 12 leaves 15 - 60cm long and a flowering scape 25 - 80cm tall from a single, underground bulb. The plant divides, forming in time a cluster of plants. The bulb is composed of a number of cloves. The plant is agreed to have evolved from the wild garlic A. longicuspis.

5. Distribution

Allium sativum is native to South Asia, Central Asia, and northeastern Iran. It grows in the wild in areas where it has become naturalized. The “wild garlic,” “crow garlic,” and “field garlic” of Britain are members of the species Allium ursinum, Allium vineale, and Allium oleraceum, respectively. In North America, Allium vineale (known as “wild garlic” or “crow garlic”) and Allium canadense (known as “meadow garlic,” “wild garlic,” or “wild onion”) are common weeds in fields.

6. Cultivation

Garlic is cultivated in many parts of the world. It is grown from cloves planted in the ground in autumn or early spring. The soil should be well-drained and rich in organic matter.

Garlic requires a cold period to grow properly. It is usually harvested in late summer or early autumn.[36]

7. Phytochemical Analysis

Garlic contains a variety of phytochemicals, including alliin, allicin, and ajoene. These compounds are responsible for the characteristic odor and flavor of garlic. Garlic also contains vitamins B6 and C, and the minerals manganese and selenium. It has been used for centuries as a traditional medicine to treat a variety of ailments, including high blood pressure, high cholesterol, and infections.

8. Medicinal Uses

- Cardiovascular Health: Garlic has been extensively studied for its potential benefits in cardiovascular health. It may help reduce blood pressure and lower cholesterol levels, contributing to heart health.
- Antimicrobial Properties: Allicin, a key compound in garlic, exhibits strong antimicrobial properties, making garlic historically valuable for combating infections.
- Immune System Support: Some studies suggest that garlic may help support the immune system, potentially reducing the severity and duration of colds and other infections.
- Anti-Inflammatory Effects: Components of garlic, including saponins and flavonoids, have anti-inflammatory properties that may be beneficial in conditions related to inflammation.
- Antioxidant Activity: Garlic's antioxidant properties may help protect cells from damage caused by free radicals, which are reactive molecules linked to various chronic diseases.[37]

2. MICROCRYSTALLINE CELLULOSE

Non-proprietary names	:	Cellulosum microcristallinum, microcrystalline cellulose
Synonyms	:	Avicel, Emcocel and Tabulose, Crystalline cellulose
Chemical Name	:	Cellulose
Empirical formula	:	$(C_6H_{10}O_5)$ n, Where n=220
Molecular weight	:	Approximately 36,000
Description	:	White, odorless, tasteless, crystalline powder
Functional category	:	Adsorbent; suspending agent; tablet and capsule diluent; tablet disintegrant.
Solubility	:	Slightly soluble in 5% w/v sodium hydroxide solution. practically insoluble in water, dilute acids, and most organic solvents
Applications	:	Adsorbent-20 to 90%, Antiadherent–5 to 20%, Capsule binder/diluents -20 to90%, Tablet disintegrant-5 to 15%, Tablet binder/diluents-20 to 90%
Stability and Storage Conditions	:	Microcrystalline cellulose is a stable though hygroscopic material. The bulk material should be stored in a well- closed container in a cool, dry place.
Incompatibilities	:	Incompatible with strong oxidizing agents
Safety	:	It is not absorbed systemically following oral administration and thus has little toxic potential.

3. MAGNESIUM STEARATE

Non-proprietary names	:	Magnesium stearate, Magnesii stearas.
Synonyms	:	Magnesium octadecanoate; octadecanoic acid, magnesium salt; stearic acid, magnesium salt
Chemical Name	:	Octadecanoic acid magnesium salt
Empirical formula	:	$C_{36}H_{70}MgO_4$
Molecular weight	:	591.34
Description	:	Magnesium stearate is a very fine, light white, precipitated or milled, impalpable powder of low bulk density, having a faint odor of stearic acid and a characteristic taste
Functional category	:	Tablet and capsule lubricant
Solubility	:	Practically insoluble in ethanol, ethanol (95%), ether and water; slightly soluble in warm benzene and warm ethanol
Applications	:	It is primarily used as a lubricant in capsule and tablet manufacture at concentrations between 0.25% and 5.0% w/w. It is also used in barrier creams.
Stability and Storage Conditions	:	Magnesium stearate is stable and should be stored in a well closed container in a cool, dry place
Incompatibilities	:	Incompatible with strong acids, alkalis, and iron salts
Safety	:	Oral consumption produces a laxative effect. No toxicity information is available.

4. TALC

Non-proprietary names	:	Purified talc, Talc, Talcum.
Synonyms	:	Altalc, hydrous magnesium calcium silicate.
Chemical Name	:	Talc
Structural formula	:	$Mg_6(Si_2O_5)_4(OH)_4$
Molecular weight	:	758.5314
Description	:	Talc is a very fine, white to greyish-white, odorless, impalpable unctuous, crystalline powder
Functional category	:	Anticaking agent; glidant diluent; tablet and capsule lubricant
Solubility	:	Practically insoluble in dilute acids and alkalis, organic solvents, and water.
Applications	:	Talc was once widely used in oral solid dosage formulations as a lubricant, diluent, and lubricant.
Stability and Storage Conditions	:	Talc is a stable material and may be sterilized by heating. at 160 ºC for not less than 1 hour. Talc should be stored in a well-closed container in a cool, dry place.
Incompatibilities	:	Incompatible with quaternary ammonium compounds.
Safety	:	Talc is not absorbed systemically following oral ingestion and is therefore regarded as an essentially nontoxic material. However intranasal or intravenous abuse of products containing talc can cause granulomas in body tissues.

5. MANNITOL

Non-proprietary names	:	Mannitol, D-Mannitol, Mannitolum
Synonyms	:	Cordycepic acid; C*PharmMannidex; E421; manna sugar;
Chemical Name	:	D-Mannitol
Molecular formula	:	$C_6H_{14}O_6$
Molecular weight	:	182.17
Description	:	Mannitol occurs as white, odourless, crystalline powder, or free-flowing granules. It has a sweet taste, approximately as sweet as glucose and half as sweet as sucrose.
Functional category	:	Mannitol is an osmotic diuretic and a pharmaceutical excipient.
Solubility	:	Soluble in water, alkalies, ethanol, glycerine, and propane
Applications	:	Diluents, diluents for lyophilized preparations sweetening agent; tablet and capsule diluent; tonicity agent.
Stability and Storage Conditions	:	Mannitol is stable in the dry state and in aqueous solutions. Solutions may be sterilized by filtration or by autoclaving and if necessary may be autoclaved repeatedly with no adverse physical or chemical effects.
Incompatibilities	:	Mannitol is incompatible with strong oxidizing agents.
Safety	:	Mannitol is a naturally occurring sugar alcohol found in animals and plants; it is present in small quantities in almost all vegetables. Laxative effects may occur if mannitol is consumed orally in large quantities (over 20g). The product label should bear the statement ‘excessive consumption may have a laxative effect.

6. EUDRAGIT L-100

Synonyms	:	Methacrylic acid
Functional category	:	Film former, tablet binder
Description	:	White powders with a faint characteristic odor.
Solubility	:	1 gm of Eudragit L-100 dissolves in 7 g methanol, ethanol, in aqueous isopropyl alcohol and acetone. Insoluble in ethyl acetate, methylene chloride, petroleum ether and water.
Applications	:	Eudragit L 100 and S 100 are employed as film coating agents resistant to gastric fluid with solubility above pH 6.0 and pH 7.0 respectively, for enteric coating of formulations. Eudragit L and S, also referred to as methacrylic acid copolymers in the USP32–NF27 monograph, are anionic copolymerization products of methacrylic acid and methyl methacrylate. The ratio of free carboxyl groups to the ester is approximately 1: 1 in Eudragit L (Type A) and approximately 1: 2 in Eudragit S (Type B).
Stability and Storage Conditions	:	Eudragit and L 100 polymers are stable at room temperature.
Incompatibilities	:	EUDRAGIT L-100 is incompatible with strong oxidizing agents.
Safety	:	Acute toxicity studies have been performed in rats, rabbits and dogs. No toxic effects were observed. Chronic toxicity studies were performed in rats over a period of 3 months. No significant changes were found in the animal organs.

7. SODIUM STARCH GLYCOLATE

Non-proprietary names :	Sodium Starch Glycolate
Synonyms :	Sodium carboxymethyl starch, Carboxymethyl starch sodium salt, Carboxymethylamylum natricum, Sodium carboxymethylated starch, Sodium carboxymethylated amylose, Sodium carboxymethylated cellulose.
Chemical Name :	Sodium carboxymethyl starch
Empirical formula :	C2H4O3·xNa·x
Molecular weight :	Variable, depending on the degree of substitution.
Description :	Sodium Starch Glycolate is a white to off-white, tasteless, odorless, relatively free-flowing powder. It is composed of the sodium salt of carboxymethyl ether. Starch glycolates are of rice, potato, wheat, or corn origin. Sodium Starch Glycolate absorbs water rapidly, resulting in swelling which leads to rapid disintegration of tablets and granules.
Functional category :	Sodium Starch Glycolate is a super disintegrant and a pharmaceutical excipient.
Solubility :	It is practically insoluble in ethanol, ether, chloroform, and other organic solvents. It dissolves in water to form a colloidal solution, which is stable to light and heat.

Applications :	Sodium Starch Glycolate is used as a pharmaceutical grade dissolution excipient for tablets and capsules. It is used as a disintegrant, a suspending agent, and as a gelling agent. Without a disintegrant, tablets may not dissolve appropriately and may affect the amount of active ingredient absorbed, thereby decreasing effectiveness.
Stability and Storage : Conditions	Stored in a cool, dry place in a well-closed container. It should be protected from light and moisture.
Incompatibilities :	Sodium Starch Glycolate is incompatible with strong oxidizing agents.
Safety :	Generally regarded as safe when used as directed in pharmaceutical formulations. Adhere to recommended handling procedures to minimize inhalation of the powder.

8. DICALCIUM PHOSPHATE

Non-proprietary names	**:**	Anhydrous Calcium Hydrogen Phosphate, Anhydrous Dibasic Calcium Phosphate
Chemical Name	**:**	Dibasic calcium phosphate
Molecular weight	**:**	136.06
Description	**:**	Anhydrous dibasic calcium phosphate is a white, odorless, tasteless powder or crystalline solid. It occurs as triclinic crystals.
Functional category	**:**	Tablet and capsule diluent.
Applications	**:**	Anhydrous dibasic calcium phosphate is used both as an excipient and as a source of calcium in nutritional supplements. It is used particularly in the nutritional/health food sectors. It is also used in pharmaceutical products because of its compaction properties, and the good flow properties of the coarse grade material.
Stability and Storage Conditions	**:**	Dibasic calcium phosphate anhydrous is a nonhygroscopic, relatively stable material. Under conditions of high humidity it does not hydrate to form the dihydrate.
Incompatibilities	**:**	Dibasic calcium phosphate should not be used to formulate tetracyline antibiotics.

9. POLYETHYLENE GLYCOL-4000

Non-proprietary names	**:**	Polyethylene glycol 4000, Macrogol 4000
Synonyms	**:**	PEG 4000, Carbowax 4000
Chemical Name	**:**	Polyethylene glycol 4000
Empirical formula	**:**	C2nH4n+2On+1
Molecular weight	**:**	3800-4200 g/mol
Description	**:**	PEG 4000 is a high-molecular-weight, water-soluble polymer that is a clear, colorless, and odorless liquid or solid, depending on the form (liquid or solid).
Functional category	**:**	PEG 4000 falls into the category of polyethylene glycols, which are used for various purposes, including pharmaceuticals, cosmetics, and industrial

applications.

Solubility	:	Highly soluble in water.
Applications	:	Commonly used as an excipient in pharmaceutical formulations, including tablet coatings, ointments, and liquid formulations. Used in the preparation of polymer- based drug delivery systems. Widely employed in the manufacturing of various cosmetic and personal care products. Used in industrial processes as a lubricant, plasticizer, and dispersant.
Stability and Storage Conditions	:	Stable under normal storage conditions. Store in a cool, dry place away from direct sunlight.
Safety	:	PEG 4000 is well-tolerated in pharmaceutical and cosmetic formulations.

10. METHYL PARABEN

Non-proprietary names	:	Methyl Paraben
Synonyms	:	Methyl 4-hydroxybenzoate, Methyl para hydroxybenzoate
Chemical Name	:	Methyl 4-hydroxybenzoate
Empirical formula	:	C8H8O3
Molecular weight	:	152.15 g/mol
Description	:	Methyl Paraben is a white crystalline powder or colourless crystals, typically odourless or having a faint characteristic odour.
Functional category	:	Methyl Paraben belongs to the class of compounds known as parabens. Parabens are esters of para-hydroxybenzoic acid and are commonly used as preservatives in pharmaceuticals, cosmetics, and food products.
Solubility	:	Methylparaben is soluble in alcohol, ether, and acetone, and slightly soluble in water.
Applications	:	Widely used as a preservative in pharmaceuticals, cosmetics, and personal care products to prevent the growth of bacteria and fungi. Commonly employed in topical formulations, oral medications, and cosmetic products like creams, lotions, and shampoos.
Stability and Storage Conditions	:	Generally stable under normal storage conditions. Store in a cool, dry place, away from heat and direct sunlight.
Safety	:	Methylparaben is generally regarded as safe for use in food, cosmetic, and pharmaceutical products. However, some people may show cross-sensitivity if allergic to local anesthetics that are metabolized to para-aminobenzoic acid.[38]

6. MATERIALS AND METHODS

MATERIALS UTILIZED

Source and Authentication of Garlic

The garlic used in this experiment was sourced from Bhavani, India. To ensure authenticity, a certificate of verification was obtained and is attached to the enclosed documentation.

Processing

The garlic cloves were meticulously peeled and dried in a hot air oven. The oven temperature was precisely controlled between 50°C and 55°C for a duration of 6 hours. Following the drying process, the garlic cloves were pulverized using an appropriate grinder to obtain a fine powder.

Botanical Information

The scientific name of the garlic used is *Allium sativum L*.

Table 4: Materials used.

Excipients and chemical	Manufacturer / Supplier
Sodium starch glycolate	Nice chemical, Mumbai.
Microcrystalline cellulose	Lobo chemie, Mumbai.
Mannitol	Lobo chemie, Mumbai.
Dicalcium phosphate	Lobo chemie, Mumbai.
Talc	Lobo chemie, Mumbai.
Magnesium stearate	Lobo chemie, Mumbai.
Methyl paraben	Merck, Mumbai.
Eudragit L-100	Lobo chemie, Mumbai.
Polyethylene glycol	Lobo chemie, Mumbai.
Acetone	Spectrum reagents and chemical, Kochi.
Diethyl phthalate	Lobo chemie, Mumbai.

Our institution serves as a primary source for the aforementioned chemicals, with additional procurement undertaken from Chemico Glass & Scientific Company Erode.

INSTRUMENTS UTILIZED

Table 5: Instruments used.

Equipment	Manufacturer / Supplier
UV Spectrophotometer	SHIMADZU Scientific instruments, Japan.
Digital Balance	Satorious 21.00 (max 220g)
Rotary tablet punching machine	Ridhi Pharma machinery, Ahmedabad, India
Hardness tester	Monsanto Hardness tester
Friability apparatus	Roche Friabilator
pH meter	Digital pH meter
Vernier calipers	Mitutoyo. Japan
Disintegration test apparatus	Servewell Industries, India
Dissolution test apparatus	Singhla apparatus
Hot air oven	Servewell Industries, India
Mechanical stirrer	Adarsh mechanical stirrer
FT-IR Spectrophotometer	SHIMADZU Scientific instruments, Japan

PREPARATION OF CALIBRATION CURVE

Determination of absorption maxima (λmax)

100 mg of garlic powder was weighed accurately and dissolved in 100 ml of methanol in 100 ml volumetric flask (stock solution). 2 ml was taken from the stock solution and transferred into 100 ml volumetric flask and diluted up to 100 ml with methanol. The resulting solution was labeled as standard working Solution. 2 ml of the working solution was withdrawn and diluted up to 10 ml with methanol in 10 ml volumetric flask. The spectrum of this solution was run in 200 to 400 nm range in UV-visible spectrophotometer. The λ max of the garlic was found to be 270 nm.

Preparation of standard graph

From above standard working solution, 1, 2, 3, 4 and 5 mL was withdrawn and diluted up to 10 ml with methanol in 10 ml volumetric flask to get concentration of 2 µg, 4 µg, 6 µg, 8 µg and 10 µg, respectively. The absorbance of each solution was measured by UV-visible spectrophotometer at 270 nm using the methanol as blank.

COMPATIBILITY STUDIES (FT-IR spectra study)

This was carried out to find out the compatibility between the garlic and excipients. 10 mg of the sample and 400 mg of KBr were taken in a mortar and triturated. A small amount of the triturated sample was taken into a pellet maker and was compressed at10 Kg/cm2 using a hydraulic press. The pellet was kept on to the sample holder and scanned in SHIMADZU FT- IR spectrophotometer. The spectra obtained were compared and interpreted for the functional group peaks.

PRECOMPRESSION PARAMETERS

Bulk density (Db)

Accurately weighed granules were carefully transferred into graduated measuring cylinder. The granules bed was then made uniform, and the volume occupied by the granules was noted as per the graduation marks on the cylinder as ml. It is expressed in gm/ml and is calculated using the following formula.

$$\text{Bulk density} = \frac{\text{Mass of powder (gm)}}{\text{Bulk volume occupied by powder (ml)}}$$

Tapped density (Dt)

It is the ratio of total mass of granule to the tapped volume of granule. The graduated measuring cylinder containing accurately weighed granule was manually tapped for 50 times. Volume occupied by the granule was noted. It is expressed in gram/mL and is calculated by following formula.

$$\text{Tapped density} = \frac{\text{Mass of powder (gm)}}{\text{Tapped volume occupied by powder (ml)}}$$

Compressibility index (I) and Hausner's ratio

Carr's index and Hausner's ratio measure the propensity of granule to be compressed and the flow ability of granule. Carr's index and Hausner's ratio were calculated using the following formula.

$$I = \frac{Dt - Db}{Dt} \times 100$$

Hausner's ratio = Dt / Db

Where, Dt – Tapped density of the powder

Db – Bulk density of the powder

Angle of repose (θ)

The frictional forces in a loose powder can be measured by the angle of repose. This is the maximum angle possible between the surface of a pile of powder and the horizontal plane. Sufficient quantities of pantoprazole granules were passed through a funnel from a particular height (2 cm) onto a flat surface until it formed a heap, which touched the tip of the funnel. The height and radius of the heap were measured. The angle of repose was calculated using the formula

$$\text{Angle of repose } (\theta) = \tan^{-1}(h/r)$$

Where, h – Height of the pile in cm, r – Radius of the pile.[39,40]

Table 6: Relationship of Angle of Repose, Carr's Index and Hausner's Ratio with flow properties of powder.

Angle of Repose	Carr's Index	Hausner's Ratio	Flow Properties
25-30	< 10	1.00 – 1.11	Excellent
31-35	11-15	1.12 – 1.18	Good
36-40	16-20	1.19 – 1.25	Fair
41-45	21-25	1.26 – 1.34	Passable
46-55	26-31	1.35 – 1.45	Poor
56-65	32-37	1.46 – 1.59	Very Poor
> 66	> 38	> 1.60	Very Very Poor

PREPARATION OF GARLIC TABLET

Preparation of garlic powder

Garlic cloves were peeled and kept in a hot air oven, temperature maintained between 50 °C to 55 °C for 6 hours. Dried garlic cloves were powdered with suitable grinder.

Preparation of powder blend

Garlic powder blend for tableting were prepared by direct compression method. Specified quantity of garlic powder, sodium starch glycolate, mannitol, dicalcium phosphate, micro crystalline cellulose and methyl paraben were weighed according to the formula (Table.7) and transferred in a mortar and pestle and mixed thoroughly. The powder was passed through sieve no 80 to obtain the granules. The specified quantity of magnesium stearate and talc were finally added and mixed for the compression of tablets.

Preparation of garlic tablets

An ideal mixture of granules was directly punched into tablets weighing about 250 mg containing 100 mg of garlic powder, using rotary tablet compression machine. The different batches of garlic tablets were collected and stored in airtight containers.

Table 7: Composition of garlic tablets.

Composition	F1	F2	F3	F4	F5	F6
Garlic (mg)	100	100	100	100	100	100
Sodium starch glycolate (mg)	2	4	6	2	4	6
Microcrystalline cellulose (mg)	27	25	23	27	25	43
Mannitol (mg)	45	70	90	40	75	70
Dicalcium phosphate (mg)	69	44	24	74	39	24
Talc (mg)	2	2	2	2	2	2
Magnesium stearate (mg)	4	4	4	4	4	4
Methyl paraben (mg)	1	1	1	1	1	1
Total Weight (mg)	250	250	250	250	250	250

COATING OF COMPRESSED GARLIC TABLETS

Preparation of enteric coating solution

The enteric coating solution was prepared by simple solution method. It was prepared by 8% W/W of Eudragit L100 as an enteric polymer, PEG 1.5% w/w as plasticizer and acetone was used as solvent. Diethyl phthalate was added and made up the volume with rest of the solvent mixture; this mixture was constantly stirred for 1h with paddle mechanical stirrer at the rate of 1000 rpm and the stirred coating solution was again filtered through muslin cloth, a coating solution was obtained.[41]

Table 8: Composition of coating solution.

Ingredients	Quantity (%)
Eudragit L100	8.0
PEG	1.5
Acetone	59.4
Diethyl phthalate	Sufficient quantity

Enteric coating of Garlic compressed tablets by dipping method

The compressed tablets were coated with enteric coating polymer (Eudragit L100) solution by dipping method. Desired tablet coating continued the dipping and weight gain was achieved. The coated tablets were studied for its weight variation, thickness, uniformity of drug content and in vitro dissolution study.[41]

POST COMPRESSION PARAMETERS

Hardness test

Tablet requires a certain amount of hardness and resistance to friability to withstand mechanical shakes of handling in manufacturing, packing, and shipping. The hardness of tablet is determined using Pfizer hardness tester. It is expressed in Kg/cm2. Three tablets are selected from each formulation and hardness of tablet is determined. The results are expressed in average value.

Thickness

Thickness tester is an instrument that measures the thickness of tablets or capsules in millimetres. To measure the tablet thickness simply place the tablet in between the jaws and slide the scale jaw to press the tablet against the stationary jaw. The reading on the display is noted and it is the actual thickness of the tablet.

Friability test

The friability was determined using friabilator and expressed in percentage (%). 20 tablets from each batch were weighed separately ($W_{initial}$) and placed in the friabilator, which was then operated for 100 revolutions at 25 rpm. The tablets were reweighed (W_{final}) and the percentage friability (F) was calculated for each batch by using the following formula.

$$\text{Friability} = \frac{(W_{initial}) - (W_{final})}{(W_{initial})} \times 100$$

Weight variation test

Ten tablets were selected at random from the lot, weighed individually and the average weight was determined. The percent deviation of each tablets weight against the average weight was calculated. The test requirements are met, if not more than two of the individual weights deviate from the average weight by more than 5% and none deviates more than 10%. IP limit for weight variation in case of tablets weighing more than 80 mg but less than 250 mg is ± 7.5%.

Drug content uniformity

The prepared garlic tablets were tested for their drug content. Three tablets of each formulation were weighed and finely powdered. About 100 mg equivalent of garlic was accurately weighed and completely dissolved in pH 6.8 phosphate buffer and the solution was filtered. 1 mL of the filtrate was further diluted to 100 mL with pH 6.8 phosphate buffer. Absorbance of the resulting solution was measured by UV spectrophotometer at 270 nm.

Disintegration time garlic tablets

Disintegration test was carried out using the tablet disintegration test apparatus pH 6.8 phosphate buffer at 37 ± 0.5 ºC was used as the disintegration media and the time in second taken for complete disintegration of the tablet.

In vitro drug release studies

Dissolution apparatus was employed to study the in vitro drug release from various formulations prepared. The dissolution medium used was 900 ml of acidic buffer of pH 1.2 for 2 h and phosphate buffer of pH 6.8 for 1 hr. The tablet was kept into the basket. The temperature was maintained at 37 ± 0.5°C and the stirring rate was 100 rpm. Samples were withdrawn at regular time intervals and the same volume was replaced with fresh dissolution medium. The samples were measured by UV spectrophotometer at 270 nm (pH 1.2) and at 270 nm (pH 6.8) against a blank. The release studies were conducted in triplicate and the mean values were plotted versus time.[42,43]

7. RESULTS AND DISCUSSION

Present study was done on enteric coating tablets with different formulation F1 to F6. Garlic were prepared by direct compression method using different concentration of, microcrystalline cellulose, mannitol, dicalcium phosphate, Sodium starch glycolate, magnesium stearate, methyl paraben and talc, Eudragit L100 were used as enteric coating polymer, which prevent drug form gastric pH and release in intestinal pH.

Determination of λ_{max}

The absorption maxima (λ_{max}) of the Garlic were estimated by scanning the drug solution between 200-400 nm region on UV spectrophotometer. The obtained spectrum showed that the absorption maxima (λ_{max}) was 270 nm in methanol which was shown in figure 5.

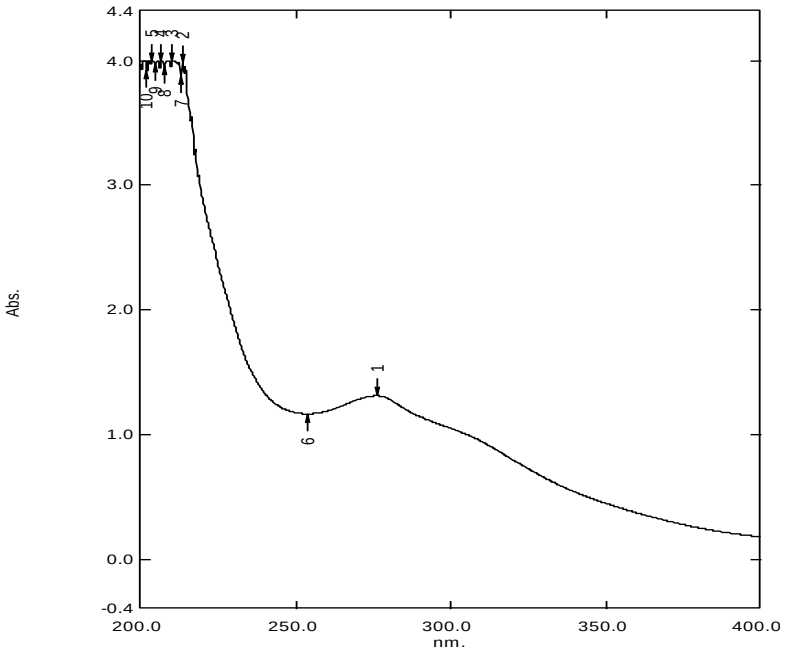


Figure 5: λ_{max} of Garlic.

Preparation of standard graphs

Standard graph for the drug garlic was done separately in methanol. Table 9 show the concentrations of garlic in methanol and the respective absorbance. The figure 6 show the calibration curves of garlic in methanol, respectively.

Table 9: Calibration data of garlic.

S. No.	Concentration (µg/ml)	Absorbance (nm)
1.	2	0.010
2.	4	0.064
3.	6	0.114
4.	8	0.161
5.	10	0.207

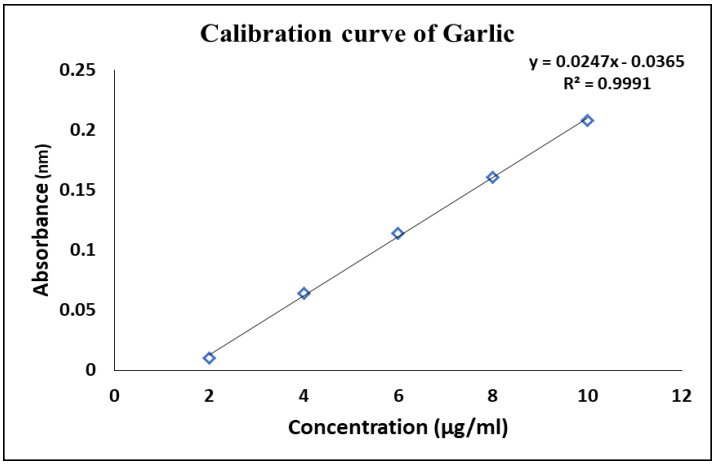


Figure 6: Standard graph of garlic.

FT-IR spectral study

FT-IR spectroscopy study was carried out separately to find out the compatibility between the Garlic and microcrystalline cellulose, mannitol, dicalcium phosphate, sodium starch glycolate, magnesium stearate, talc, methyl paraben. The FT-IR was performed for drug, polymer and the physical mixture of drug-polymer. The spectral obtained from FT-IR spectroscopy studies shows in figures 7-10.

The peaks obtained in the spectra of drug and polymers mixtures correlates with each other. This indicates that the drug was compatible with the formulation components. IR studies indicated no interaction between drug and polymers.

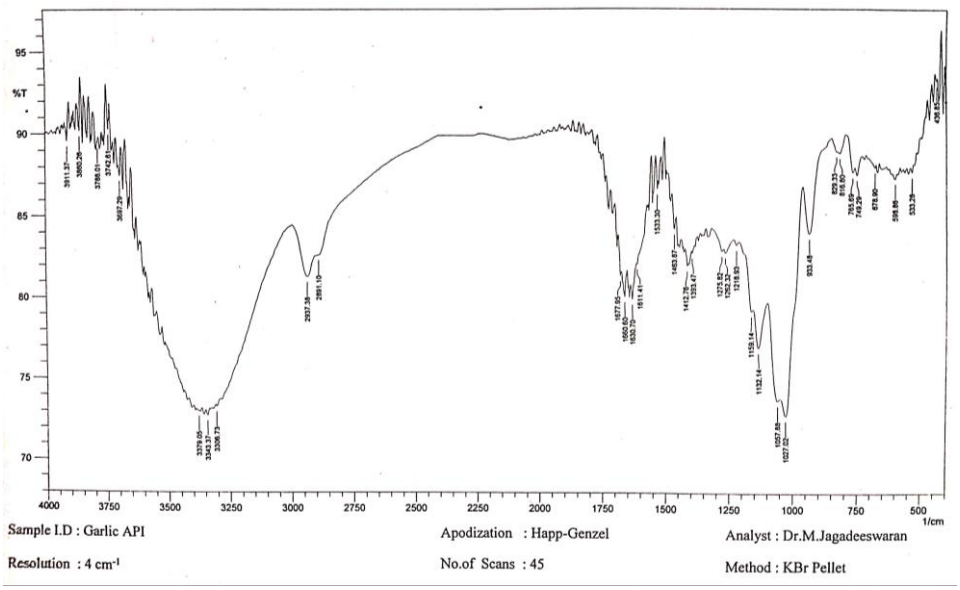


Figure 7: FT-IR Spectrum of Garlic.

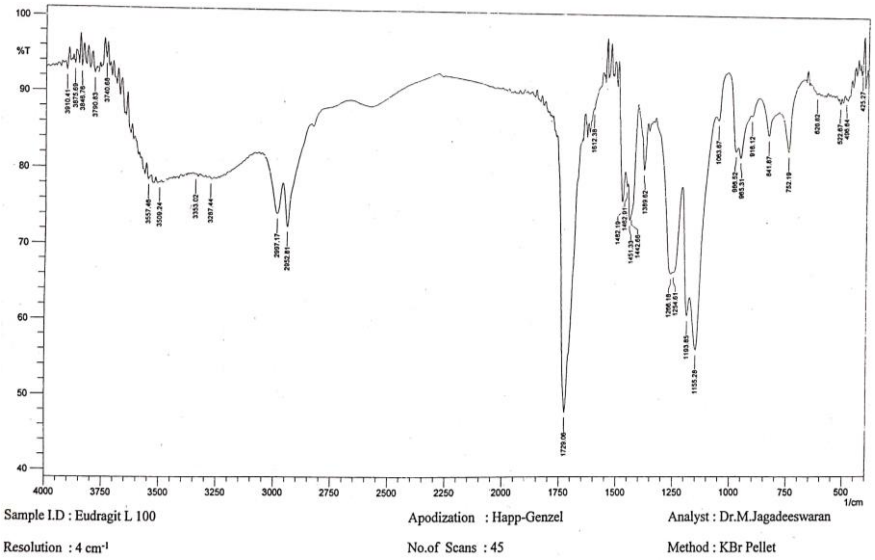


Figure 8: FT-IR Spectrum of Eudragit L100.

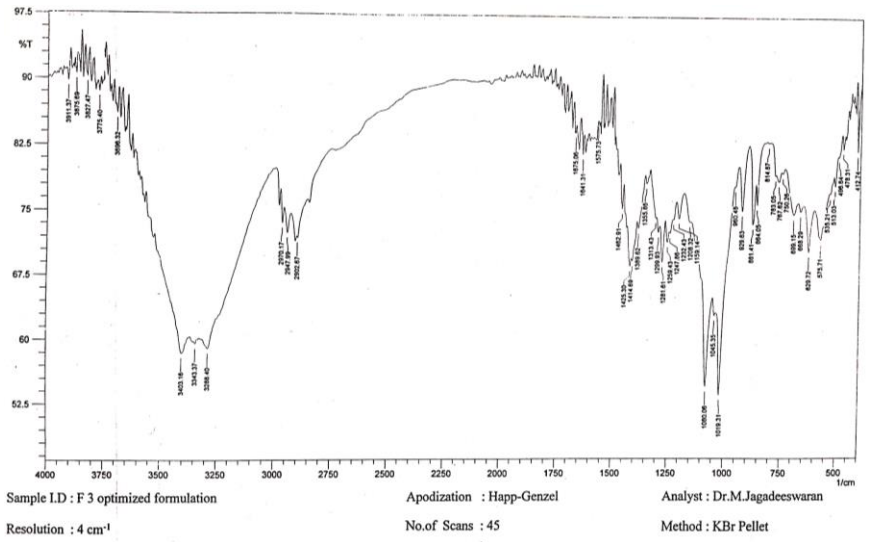


Figure 9: FT-IR Spectrum of physical mixture.

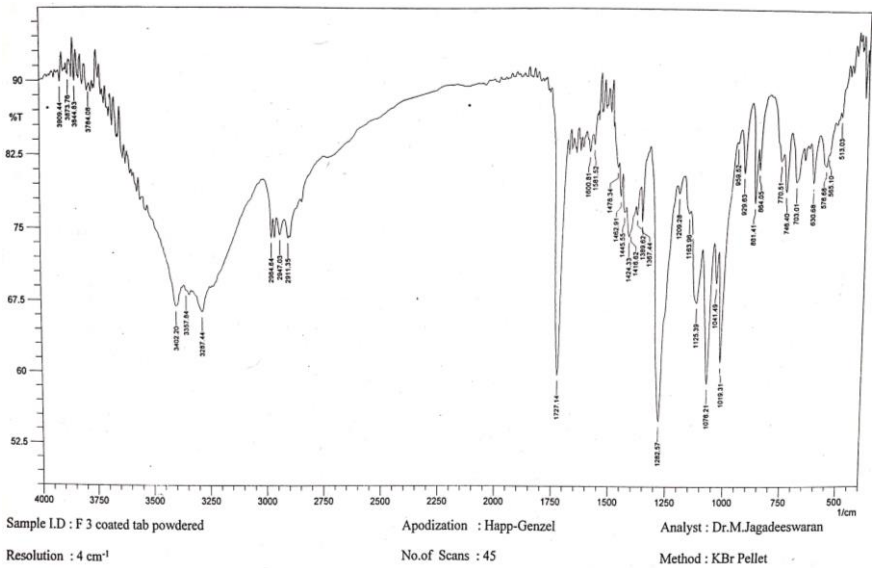


Figure 10: FT-IR Spectrum of Coated tablet.

Garlic enteric coated tablets images

Figure 11: Formulation 1.

Figure 12: Formulation 2.

Figure 13: Formulation 3.

Figure 14: Formulation 4.

Figure 15: Formulation 5.

Figure 16: Formulation 6.

EVALUATIONS

Precompression parameters

The prepared garlic powder blend for tabletting was prepared by direct compression method. The prepared garlic powder blend was evaluated angle of repose, bulk density, tapped density, Hausner's ratio and compressibility index as given on Table 10. The bulk densities of the granules were found to be in the range of 0.671 to 0.738 gm/ml, while the tapped densities were ranged between 0.849 to 0.918 gm/ml. The flow characteristics of the granules were assessed by determining their Angle of repose, Carr's Index and Hausner's ratio. The values of compressibility index are 18.00 to 23.42 that signify fair and passable flowability. The values of Hausner's ratio are 1.21 to 1.30 that signify fair and passable flowability. The angle of repose of all formulation was less than 36º the value is 32.41 to 35.53 that also indicate the good and fair flowability of the prepared granules.

Table 10: Pre compression parameters of Garlic.

Formulation Code	Parameter				
	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's Index	Hausner's Ratio	Angle of repose (Ɵ)
F1	0.692	0.849	18.49	1.22	32.74
F2	0.703	0.900	21.88	1.28	32.41
F3	0.738	0.900	18.00	1.21	33.69
F4	0.703	0.918	23.42	1.30	35.53
F5	0.671	0.865	22.42	1.28	34.59
F6	0.692	0.900	23.11	1.30	32.82

Post compression parameters

The garlic tablets were prepared by direct compression method and were evaluated for their hardness, thickness, weight variation, content uniformity, friability, disintegration time and in vitro drug release (Table 11).

The average hardness of the tablets to be in range was found within 7.80 to 8.20 Kg/cm2. The average thickness of the tablets to be in range was found within 4.00 to 4.26 mm. Friability value which also affected by the hardness value of tablets should be in the range 1% limits, which is the usual friability range of tablets. The friability of the prepared tablets was found less than 1% w/w. The drug content uniformity of garlic present in tablets formulation ranged from 95.62 to 98.17. The average weight found 247 to 254 mg. Disintegration time varied between 25.30 to 33.15, hence all shows favorable result.

Table 11: Post compression parameters of Garlic core tablet.

Formulation Code	Parameter					
	Hardness (Kg/cm2)	Thickness (mm)	Friability (%)	Weight variation (mg)	Drug content (%)	Disintegration time (min)
F1	8.00	4.10	0.67	248	96.28	28.15
F2	7.80	4.24	0.51	247	97.12	31.25
F3	7.90	4.00	0.47	251	98.17	25.30
F4	8.20	4.14	0.63	253	96.50	30.10
F5	8.10	4.20	0.71	254	95.62	29.40
F6	8.10	4.26	0.70	249	97.10	33.15

In vitro drug release studies of enteric coated tablets

The in vitro release of Garlic from the prepared tablets was studied in pH 1.2 for 2 h and in phosphate buffer pH 6.8 for 1 h. In vitro dissolution studies were performed by using acidic buffer of pH 1.2 and phosphate buffer of pH 6.8 as a

dissolution medium. Formulation which shows most satisfactory result is F3, where drug release started after 2 hrs, and released maximum 98.58 by 3 hrs. Remaining were respectively, released started and reached maximum, F1-90 min and 93.42 in 3 hrs, F2-2 hrs and 90.16 in 3 hrs, F4- 105 min and 95.71 in 3 hrs, F5-105 min and 91.85 in 3 hrs, F6-105 min and 93.46 in 3 hrs. The cumulative percentage releases of garlic from the tablets were shown in Table 12 and Figure 17.

Table 12: In vitro drug release of Garlic tablet.

Time (min)	Cumulative percentage drug release					
	F1	F2	F3	F4	F5	F6
15	0	0	0	0	0	0
30	0	0	0	0	0	0
45	0	0	0	0	0	0
60	0	0	0	0	0	0
75	0	0	0	0	0	0
90	0	0	0	0	0	0
105	14.62	0	0	0	0	0
120	36.58	0	0	13.19	19.31	16.55
135	54.05	38.67	33.24	44.62	36.84	37.64
150	71.91	56.16	59.73	67.83	60.52	64.92
165	84.46	74.82	87.42	85.38	76.63	81.73
180	93.42	90.16	98.58	95.71	91.85	93.46

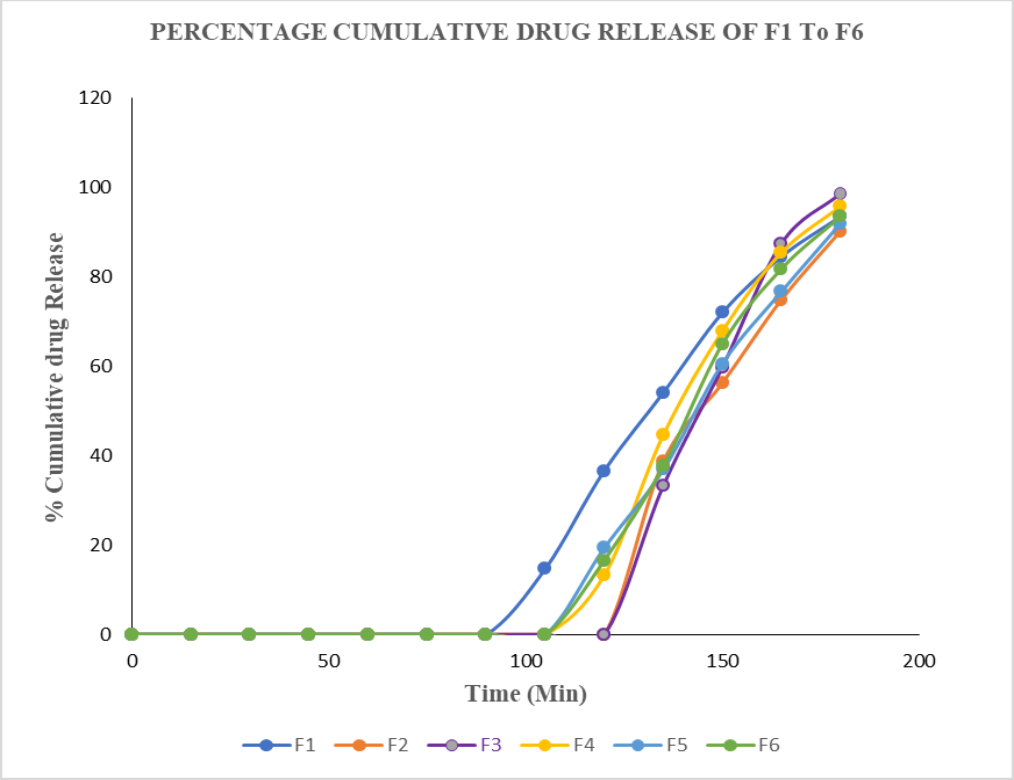


Figure 17: Percentage cumulative drug release of F1 to F6.

8. CONCLUSION

Based on your findings that F3 with a high percentage of sodium starch glycolate exhibited the best performance among your six garlic enteric-coated tablet formulations, this is due to:

1. Optimization of Sodium Starch Glycolate

F3 demonstrates the optimal concentration of sodium starch glycolate for achieving desired tablet characteristics in your specific garlic enteric-coated tablet formulation.

2. Comparison with Existing Products

Comparing the performance of F3 with commercially available garlic tablets. This involves evaluating parameters like disintegration time, dissolution profile, allicin stability, and potential side effects. This comparison can highlight the potential advantages of our optimized formulation.

Hence the enteric-coated garlic tablets represent a promising and innovative approach for delivering the therapeutic benefits of garlic to patients with neurodegenerative diseases. The enteric coating effectively protects the garlic extract from degradation in the stomach, allowing for its targeted release and absorption in the small intestine. This optimized delivery system resulted in significantly improved bioavailability of bioactive compounds like allicin and S-allylcysteine compared to conventional garlic preparations.

Furthermore, the enteric coating significantly reduced the gastrointestinal side effects associated with raw garlic consumption, making the tablets more palatable and tolerable for long-term use. The tablets exhibited significant antioxidant, anti-inflammatory, and anti-apoptotic effects, suggesting their potential to prevent or delay the progression of neurodegenerative diseases like Alzheimer's and Parkinson's disease.

Overall, the formulated enteric-coated garlic tablets offer a safe, effective, and convenient way to harness the therapeutic potential of garlic for neurodegenerative disease management.

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