FORMULATION AND EVALUATION OF BOSWELLIA SERRATA AND ALOE VERA MICROSPHERE FOR ULCERATIVE COLITIS TREATMENT

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by

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to the

Faculty of Pharmacy

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(Formerly Uttar Pradesh Technical University) LUCKNOW

July, 2024

DECLARATION

I hereby declare that the work presented in this report entitled **"Formulation And Evaluation of Boswellia Serrata And Aloe Vera Microsphere For Ulcerative Colitis Treatment"**was carried out by me. I have not submitted the matter embodied in this report for the award of any other degree or diploma from any other University or Institute. I have given due credit to the original authors/sources for all the words, ideas, diagrams, graphics, computer programs, experiments, and results, that are not my original contribution. I have used quotation marks to identify verbatim sentences and given credit to the original authors/sources. I affirm that no portion of my work is plagiarized, and the experiments and results reported in the report are not manipulated. In the event of a complaint of plagiarism and the manipulation of the experiments and results, I shall be fully responsible and answerable.

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Formulation and Evaluation of Boswellia Serrata and Aloe Vera Microsphere For Ulcerative Colitis Treatment

Pooja Sharma

'ABSTRACT'

Ulcerative colitis (UC) is a chronic inflammatory bowel disease characterized by inflammation and ulceration of the colon and rectum. Conventional treatments often fall short of providing sustained relief and may be associated with adverse effects. Natural products like Boswellia serrata and Aloe vera have demonstrated promising anti-inflammatory and wound-healing properties, making them potential candidates for UC management.

This study aimed to develop and evaluate microspheres containing Boswellia serrata and Aloe vera extracts for targeted delivery and enhanced therapeutic efficacy in UC. Microspheres were prepared using a biocompatible polymer through the Spray dryingtechnique. The formulations were optimized based on particle size, drug loading efficiency, and in vitro release profiles.

Characterization studies including scanning electron microscopy (SEM), Fourier-transform infrared spectroscopy (FTIR), and differential scanning calorimetry (DSC) confirmed the successful encapsulation of Boswellia serrata and Aloe vera extracts within the microspheres without altering their chemical integrity. The optimized formulations exhibited spherical morphology with uniform size distribution.

In vitro release studies demonstrated sustained release of Boswellia serrata and Aloe vera extracts from the microspheres over an extended period, suggesting their potential for prolonged therapeutic action. Furthermore, the microspheres exhibited pH-responsive release behavior, indicating targeted delivery to the inflamed regions of the colon.In conclusion, the formulated Boswellia serrata and Aloe vera microspheres hold significant promise as a novel approach for the management of ulcerative colitis, offering targeted delivery, sustained release, and the potential for enhanced therapeutic efficacy while minimizing adverse effects.

Keywords: Boswellia serrata, Aloe vera, Microspheres, Inflammation.

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POOJA SHARMA

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LIST OF ABBREVIATION

UC: Ulcerative Colitis

BS: Boswellia Serrata

AV: Aloe Vera

IBD: Inflammatory Bowel Disease

SEM: Scanning Electron Microscopy

FTIR: Fourier Transform Infrared Spectroscopy

DSC: Differential Scanning Calorimetry

pH: Potential of Hydrogen

NDDS: Novel Drug Delivery System

CR: Controlled Release

IR: Immediate Release

PEG: Polyethylene Glycol

PMMA: Polymethyl methacrylate

DNA: Deoxyribonucleic Acid

$CaCl_2$: Calcium dichloride

PVA: Polyvinyl Alcohol

LH-RH: Luteinizing Hormone Releasing Hormone

PLA: Polylactic Acid

ESR: Erythrocyte Sedimentation Rate

CRP: C Reactive Protein

E coli: Escherichia Coli

DCM: Dichloromethane

IBS: Irritable Bowel Syndrome

HPMC: Hydroxy Propyl Methyl Cellulose

FDA: Food and Drug Administration

EMA: European Medicines Agency

NMT: Not more than

NLT: Not less than

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CHAPTER- 1

INTRODUCTION

1.1.NOVEL DRUG DELIVERY SYSTEM

The need to get past the restrictions of conventional approaches has prompted the change of medication delivery systems. Improved efficacy, increased patient compliance, controlled release, and less administration frequency and costs are just a few of the benefits of new drug delivery systems. In terms of product innovation and market expansion, these developments not only help consumers but also provide major chances for pharmaceutical corporations. As technology develops constantly, new medication delivery techniques should become even more important in the pharmaceutical sector.

1.2.NEED FOR NOVEL DRUG DELIVERY SYSTEM

Conventional dosing forms of medications generate an instantaneous release that results in oscillation of plasma drug levels. A new drug delivery method is required to optimize therapeutic advantages and reduce side effects while preserving the concentration of the medication inside the therapeutic range. Many pharmaceuticals, including peptides, proteins, antibodies, vaccinations, and gene-based drugs, cannot be absorbed utilizing traditional paths due of enzymatic breakdown, poor bioavailability, and poor penetration of the intestinal mucosa. Only injections allow one to use protein and peptide medications. A new medication delivery mechanism has been designed and presented to solve these drawbacks. Conventional dosing forms of medications generate an instantaneous release that results in oscillation of plasma drug levels. A new drug delivery method is required to optimize therapeutic advantages and reduce side effects while preserving the concentration of the medication inside the therapeutic range. Many pharmaceuticals, including peptides, proteins, antibodies, vaccinations, and gene-based drugs, cannot be absorbed utilizing traditional paths due of enzymatic breakdown, poor bioavailability, and poor penetration of the intestinal mucosa. Only injections allow one to use protein and peptide medications. A new medication delivery mechanism has been designed and presented in order to solve these drawbacks.

1.3.IDEAL FEATURES

1. Drug delivery systems find nanoparticles appealing because of their various desired properties.
2. Achieved by coating them with compounds like polyethylene glycol (PEG) to lower immune recognition, these properties include biocompatibility and non-immunogenicity.
3. Furthermore built with sturdy structures and surface changes to improve physical and chemical stability in physiological settings are nanoparticles.
4. Targeting utilizing nanoparticles functionalized with ligands or antibodies that identify particular receptors or markers on target cells guarantees accuracy.
5. Standardizing manufacturing techniques helps to guarantee uniformity in the generation of medication delivery systems based on nanoparticles.
6. Through several processes like diffusion, degradation, or stimuli-responsive release, nanoparticles can be designed to deliver medications in a regulated manner.
7. Correct surface changes and encapsulation help to reduce drug leaking during transit.

8. Drugs can be delivered via nanoparticles without aggravating disease progression or generating negative effects.
9. Moreover, several methods of synthesizing nanoparticles are rather quick and can be expanded for reasonably cheap manufacturing.

1.4 Advantages

1. Under control by keeping target medication concentration and controlled rate,
2. correct dosage,
3. improved performance and security,
4. Drug delivery tailored to sites or targets with an ideal dosage,
5. less side effects and toxicity,
6. raising patients' comfort and standard of living.

Disadvantages

1. First, one should pay attention to bio-acceptability restrictions.
2. Second, manufacturing nanoparticles on a big scale can prove difficult.
3. Furthermore challenging to handle in both liquid and dry state are the small size of the particles and their great surface area.
4. Aggregation of particles can thus be difficult.
5. Moreover, limited load and explosion can help to explain the small particle size and great surface area.
6. Thus, the pragmatic problems must be resolved before nanoparticles can find use either commercially or therapeutively.
7. Last but not least, the present work advances surface manipulation, drug loading techniques, release control, and potential uses of drug delivery systems for nanoparticles.

1.5Future Prospects and Opportunities in India

The pharmaceutical industry depends heavily on India, so many global behemoths have showed a strong desire in investing in and expanding in this industry. New and sophisticated methods developed in the field of Novel Drug Distribution Systems (NDDS) will generate a great need for a range of excipient use and development. India is well-known for its fast adaptation to new excipients and related technologies. Consequently, the market for excipients in India will develop in two directions: first, exporting novel organic excipients; second, using new excipients in different sophisticated delivery systems.

Most pharmaceutical corporations in the nation have been requesting and getting fresh patents in the field of novel drug delivery systems. This will therefore lead to a great demand for the goods and services provided by pharmaceutical and related companies in not too distant future. Various recent applications of nanotechnology in new drug delivery systems could perhaps enhance the diagnosis, therapy, and post-administration monitoring of medication composition within the human systems. Computer-aided drug

design is another significant milestone to be discussed here since it provides a great platform for the evolution of this kind of innovative and sophisticated systems. By means of better precision and quality than conventional approaches, computer-aided drug design aids in designing and developing medications and delivery systems consuming less time and resources.

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1.6 Recent developments in novel drug delivery system

1. Phytosome
2. Liposome
3. Nanoparticles
4. Nano emulsions
5. Microsphere
6. Ethosome
7. Niosomes
8. Proniosomes

1.7PROPERTIES & APPLICATION

1.7.1 Phytosome

A new method for administering natural medications, phytosomes present a viable solution. These result from phosphatidylcholine combined with polyphenolic phytoconstituents. The resultant system covers the active citizens and shields them from bacterial and digestive secretions' destruction. Phytosomes also enable absorption from a water-loving environment into the lipid-loving environment of cell membranes, therefore enabling them to enter the bloodstream eventually. Phytosomes have one of fundamental advantages since they preserve the therapeutic efficacy of active phytocompounds by maintaining their integrity. Studies have demonstrated that phytosomes improve bioavailability over traditional herbal extracts, therefore producing improved pharmacokinetic and therapeutic characteristics. Phytosomes thus have great potential to treat many ailments without sacrificing the efficacy of natural chemicals.

Properties of Phytosomes:

Chemical Properties:

1. Phytosomes are complexes between a natural substance and natural phospholipids, such soy phospholipids.
2. Like complexes develop by the interaction of stoichiometric amounts of phospholipids with the chosen polyphenol, like simple flavonoids, in a nonpolar solvent.

3. Hydrogen bonds between the polar groups of phospholipids and the polar section of the substrate molecule develop during this interaction.[62]

Biological Properties:

- The biological activity of phytosomes has been clarified by pharmacokinetic and pharmacodynamic research in experimental animals and human patients. These features draw attention to the chemical complexity and biological activity of pyrosomes, therefore suggesting their possibility for improved therapeutic efficacy and drug delivery.

Method of preparation

The general method of preparing pyrosomes involves several steps:

1. Usually 1:1, phospholipids and the substrate—such as herbal extracts—are combined in an appropriate ratio under the presence of an aprotic solvent. Among aprotic solvents include acetone and dioxane.

2. Complex Isolation: The developed complex is isolated by precipitation technique. There are several ways one can precipitate, including:

- Lyophilization (freeze-drying)
- Use of aliphatic hydrocarbons
- Spray drying method
- Drying of phytosomes
- Hydration of prepared phytosomes to obtain a phytosomal suspension.

3. Usually made by adding the necessary phospholipid—such as soy lecithin—to plant extracts in an aprotic solvent, phytosomes are One main component in soy lecithin is phosphatidylcholine, which has two purposes. While the choline section is hydrophilic—that is, water-loving—the phosphatidyl section is lipophilic—that is, fatty. While the phosphatidyl component interacts with lipid-soluble chemicals to create a complex with increased stability and bioavailability, the choline portion interacts with hydrophilic active ingredients.

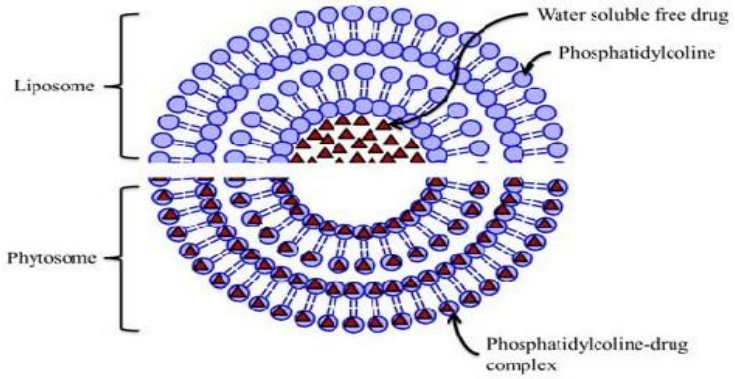

Fig.1.1 Structure of Phytosome

1.7.2 Liposomes:

Comprising one or more concentric spheres of lipid bilayers encircling aqueous compartments, liposomes are flexible structures. Because they can encapsulate both hydrophilic and lipophilic substances while preserving stability, they are extensively used in many sectors including cosmetics, drugs, food, and agriculture. Their benefits, characteristics, and techniques of preparation are broken forth below.

Advantages of Liposomes:

1. Encapsulation of lipophilic and hydrophilic medicinal compounds.
2. Good solubilization capability.
3. Perfect biological, chemical, and colloidal stability.
4. Reduction in macrophage absorption.
5. Improvement of encapsulated medication therapeutic efficacy.
6. Maintenance of therapeutic medication levels in the circulation.
7. Drug protection from environmental elements.
8. Encouragement of drug molecule intracellular distribution.

Properties of Liposomes:

1. Liposomes are formations comprising bimolecular sheets intercalated by aqueous space.
2. Like water, permeable
3. Sensitive osmotically.
4. While negative charged membranes are quite permeable to anions, positively charged membranes are impenetrable to cations.

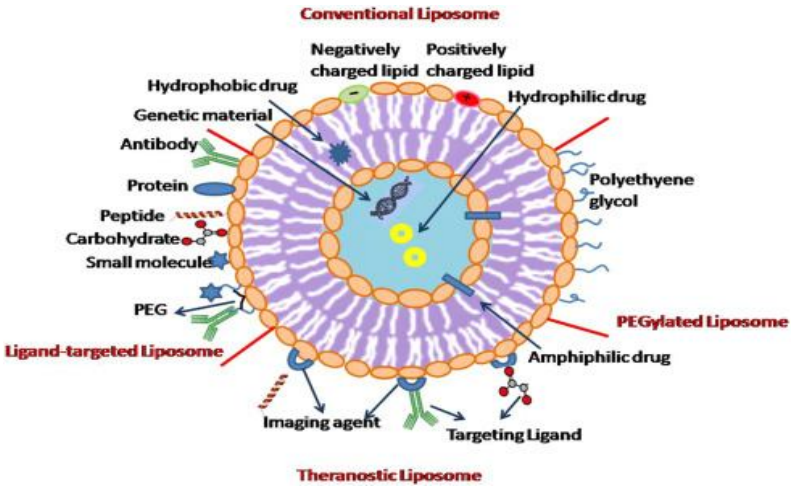

Fig.1.2 Structure of Liposome

1.7.3Nanoparticles:

Usually measuring between 10 and 1000 nanometers, nanoparticles are classified as solid particles or particulate dispersions. Drugs either dissolved, entrapped, encapsulated, or linked to their matrix can be carried by them. Existing in the solid state, nanoparticles—which range in size from 10 to 200 nm—nanospheres and nanocapsules—can be either amorphous or crystalline. Usually used for their preparation, polymeric materials produce either nanospheres or nano capsules depending on the technique used.

Advantages of Nanoparticles:

1. Features of degradation controlled by matrix ingredients. Biodegradability; non-toxicity; site-specific targeting; long-term storage capacity.
2. Particle controlled medication release
3. Improved pharmacological reaction per unit dosage and therapeutic efficacy.
4. More medicines' or proteins' stability against enzymatic breakdown.
5. Attaching ligands to the particle surface allows targeted medication delivery to particular bodily locations.
6. High drug loading capacity sustaining drug activity without chemical reactions.

Properties of Nanoparticles:

1. High surface area to- volume ratio, causing diffusion—particularly at high temperatures.
2. Special optical characteristics resulting from quantum interactions; gold nanoparticles in solution have a red-to- black hue.
3. Stability of suspension resulting from robust contact between particle surface and solvent.
4. Effective for stabilizing emulsions, formation of Janus particles with one hydrophilic and one hydrophobic half

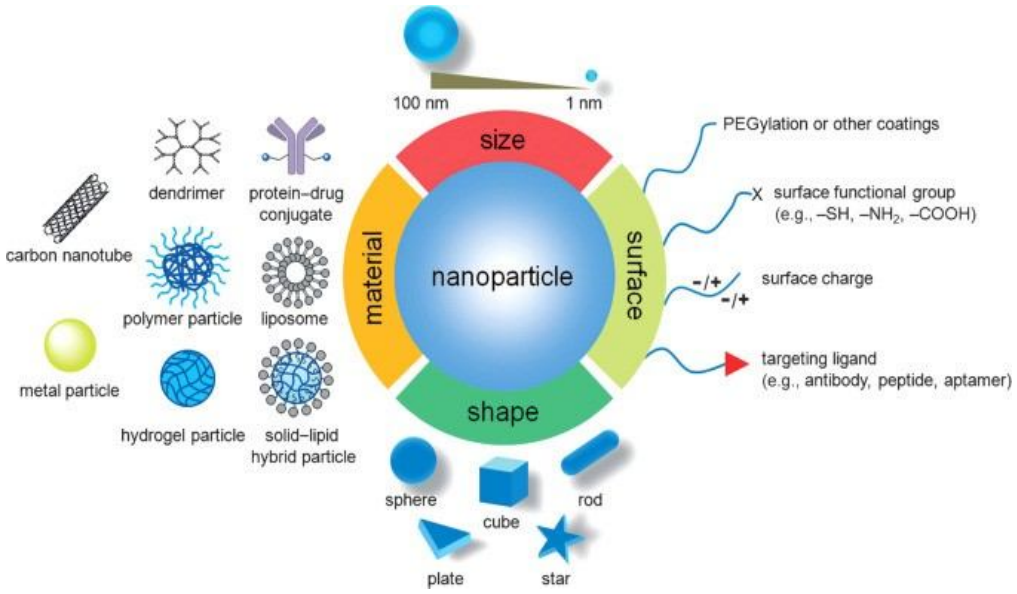

Fig.1.3 Structure of Nanoparticle

1.7.4 Niosomes:

Comprising non-ionic surfactants, niosomes are multilamellar vesicular structures that resemble liposomes but substitute non-ionic surfactives for phospholipids. These vesicles may entrap both hydrophilic and hydrophobic solutes and have attracted interest as a substitute for liposomes.

Advantages of Niosomes:

1. Improved therapeutic impact and patient compliance above standard oily formulations.
2. Versatility in drug delivery, able to entrapped amphiphilic, lipophilic, and hydrophilic pharmaceuticals.
3. Drugs released under control and sustainability resulting from depot development.
4. Customized drug delivery requires controllable shape, size, content, and fluidity of niosomes.
5. Improved bioavailability than in more traditional dosing formulations.
6. effective medicine targeting towards different organs.
7. more stability than liposomes.
8. Drugs' increasing penetration via the skin.

Properties of Niosomes:

Biodegradable, biocompatible, nonimmunogenic surfactant-based niosomes exist.Acting as a drug depot in the body, they release pharmaceuticals under control through their closed bilayer structure, therefore producing a continuous release of the encapsulated

drug to the target site. Reduced clearance and targeted therapy help medications contained in niosomes have therapeutic benefits. With their hydrophilic, amphiphilic, and lipophilic character, niosomes can fit a great range of pharmaceuticals with different solubility. Usually for humans, niosomes are not harmful. Different kinds of additives used combined with the medicine contained in niosomes helps to increase niosome stability. For example, adding cholesterol gives niosomes stability and helps to lower leakage in them.

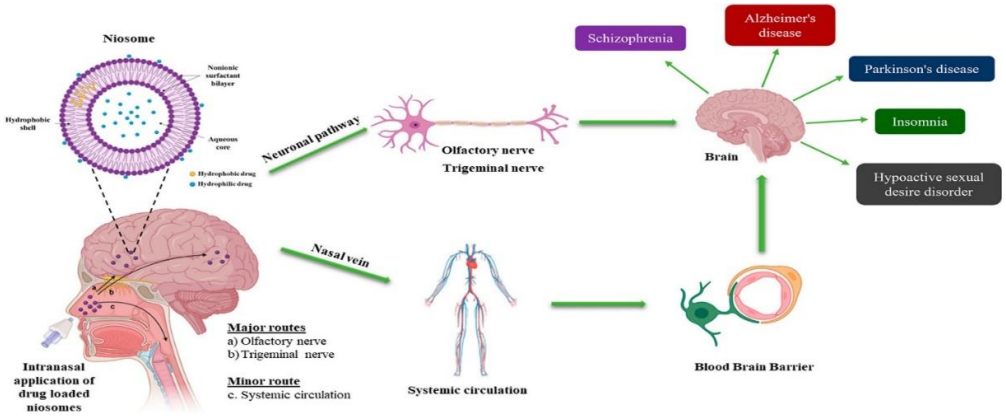

Fig.1.4 Structure of Niosomes

1.7.5Nano emulsions

Usually spanning 10 to 1000 nm, nano emulsions are colloidal particulate systems with submicron size range particles. Drug molecules find solace in them, which also improves therapeutic efficacy by means of stability and lowers side effects. Treatment of infections of the reticuloendothelial system (RES), enzyme replacement therapy in the liver, cancer treatment, and vaccination all benefit from these systems especially.Deviations from emulsions: Generally in terms of size and shape of the particles in the continuous phase, nano emulsions differ from ordinary emulsions (macroemulsions). Comparatively to ordinary emulsions (0.1–100 μm), nano emulsions have much smaller particle sizes (5–200 nm).

Advantages of Nanoemulsions:

1. Gives water-insoluble medicines an aqueous dosage form.
2. Gowers absorption variance.
3. Increases bioavailability.

4. Resists sedimentation, flocculation, coalescence, and creaming.
5. Improves absorption speed.
6. Helps lipophilic medications be soluble.

Properties of Nano emulsions:

Among its special qualities are small droplet size, great stability, translucent appearance and adjustable rheology via nano emulsions. These qualities make nano emulsions a desirable target**.**

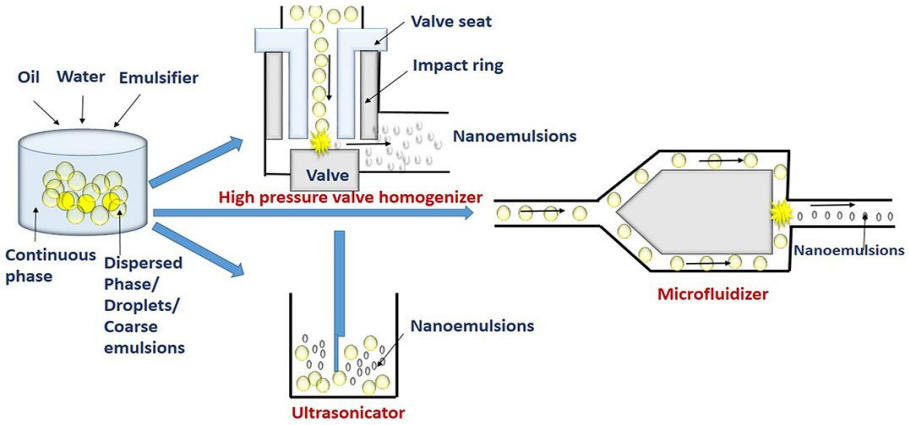

Fig.1.5 Micro fluidization technique

1.7.6 MICROSPHERE

Little spherical particles with diameters ranging from 1 μm to 1000 μm, microspheres—also called microparticles—range in One can create them from several natural and manmade materials like ceramic, polymer, and glass. varied densities of solid and hollow microspheres allow them varied applications.[62]

Among the most often used polymer microspheres are polyethylene and polystyrene ones. Because they help such activities, polystyrene microspheres are very helpful in biomedical operations such cell sorting and immunoprecipitation. On them, proteins and ligands will readily and permanently adsorb.

Essential parts of medication delivery systems, microspheres provide focused distribution of therapeutic agents together with controlled release. Attaching pharmaceuticals to microspheres lets one control drug behavior in vivo, so affecting aspects including

clearance kinetics, tissue distribution, metabolism, and cellular interaction, so improving therapeutic efficacy and reducing side effects.[62]

Gastretentive dosage forms and oral controlled drug delivery systems have been developed to improve drug bioavailability and prolong drug release in the gastrointestinal tract. These advances aim to reduce side effects and toxicity by delivering drugs in optimum dosages to target tissues over the right duration.

From biological applications to drug delivery systems, microspheres are finally adaptable tools with precision control over drug dispersion that increase therapeutic efficacy in many different industries.

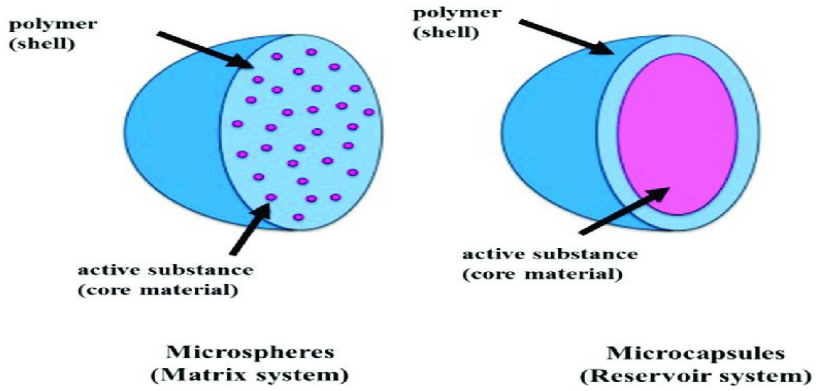

Fig.1.6. Structure of Microspheres

Characteristics:

In traditional diagnosis, the particle size is usually determined by the test or assay form. Although larger, cell-sized spheres of around 4-10 μm are ideal for bead-based flow cytometric experiments, tiny spheres of roughly 0.1-0.4 μm are used to obtain suitable woking in lateral flow tests.

Microspheres are usually made of silica, poly(methyl methacrylate), (PMMA), and polystyrene (PS). These materials have different optical and physical properties, hence depending on their use they could be either beneficial or limiting. Usually polymer beads are hydrophobic and highly protein binding.

Microspheres can be covered in diagnostic or separation settings with capture molecules like peptides, oligonucleotides, and antibodies. Usually aiming for the target specialized activity, microsphere coatings reduce nonspecific interactions. Three basic coating techniques: adsorption, covalent coupling, and affinity binding are supported by standard microsphere products.

Many popular products are suitable for this; polymer spheres and polymer-based magnetic spheres are usually internally colored using organic solvent swelling. One can create beads with varying brightness depending on individual demands by varying the dye concentrations.

Advantages

Little particles called microspheres offer a continuous, long-lasting therapeutic impact.

By helping to lower the frequency of medicine dosage, they increase patient compliance.

Microspheres can be injected into the body since of their small size and spherical form.

Microspheres help to improve drug use by increasing the bioavailability of medications and therefore lowering the incidence or strength of side effects.

Microspheres' shape lets one manage the diversity in medication release and breakdown, which would help in treatment.

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Limitation

1. You should be aware of several flaws in controlled-release formulations, among which:
2. The release from these formulations might not be constant always.
3. Meal consumption and transit through the intestines are two of the many elements that affect the rate of release of the controlled release dose form.
4. One dose to another the release rate could differ.
5. The usual larger dosage of medicine is offered by controlled-release formulations. Toxic effects are likely to occur in the event that the dosage form loses any of its releasing properties.
6. One should not chew or crush forms of this kind.

Applications

Microspheres produced from polymers such as chitosan are quite important for several pharmacological uses particular to drug delivery systems.

1. One such use for polymer-based systems such hydrogels is ophthalmic medication administration, where its bio adhesive and permeability-enhancing characteristics are utilized. These systems enable medications to enter deeper and stay on the surface of the eye for more time. Drugs include indomethacin and cyclosporine have showed promise in chitosan-based colloidal systems and microspheres delivering to the eye.
2. Because of their simplicity of manufacture, low immunological reaction, and ability to target particular cells or tissues, polymer carriers—including chitosan—also find usage in gene therapy. As seen by chitosan passing luciferase genes to the intestinal tract, they can provide plasmid DNA.

3. Microspheres and polymer films are applied for localized drug delivery in cancer treatment. For continuous medication release at tumor locations, for example, paclitaxel-loaded polymer films and microcapsules have been produced.
4. Oral medication delivery has promise from polymer films and microparticles. To give controlled release of medications like diazepam, they can be formed film dosage forms or be included into tablets. Polymers fit oral delivery uses because of their mucoadhesive qualities and pH sensitivity.
5. Because of its bio adhesive qualities, polymer-based systems like microspheres, liposomes, and gels are often employed for nasal and buccal medication delivery. They improve residence duration and medication absorption quite successfully. For instance, formulations based on chitosan have shown efficacy delivering insulin and vaccinations.
6. Microspheres and coated capsules made of polymer-based systems are recommended in gastrointestinal and colonic medication delivery. By means of controlled release and focused administration to particular areas of the GI tract, they can help to lower systemic adverse effects and increase therapeutic efficacy.
7. Modified polymer systems such as thiolate chitosan are employed in vaginal medication administration. They increase mucoadhesion and slow down medication release. Likewise, since chitosan-based films and gels provide consistent medication release—including lidocaine hydrochloride—they are appropriate for transdermal delivery.
8. Another handy multi-particulate delivery approach are chitosan pellets made with extrusion/spherization technique. They could help to raise patient compliance and treatment efficacy.

1.8 TECHNIQUES OF MICROSPHERE

1.8.1 Spray Drying Technique

Dissolving the polymer in a volatile organic solvent—such as dichloromethane or acetone—is known as spray drying. High-speed homogenization then distributes the solid medication among the polymer solution. Then, atomized in a stream of hot air, this dispersion creates a fine mist or small droplets. Microspheres produced via instant solvent evaporation vary in size from 1 to 100μm. While the cyclone separator isolates the microparticles from the hot air, vacuum drying removes trace of solvent. This quick method under aseptic conditions generates porous microparticles, which makes it advantageous.[62]

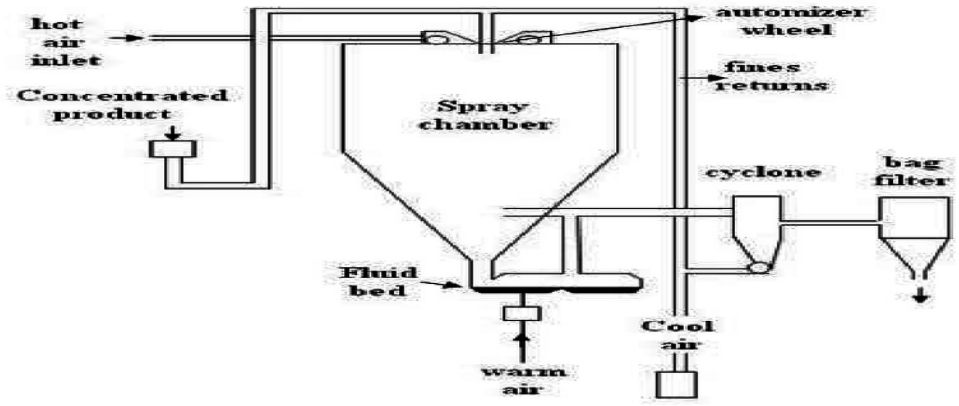

Fig. 1.7 Spray Drying Technique

1.8.2 Wet Inversion Technique

From a nozzle, drop a chitosan solution in acetic acid into an aqueous counter ion sodium tripolyphosphate solution. The resulting microspheres were permitted to stand for one hour before cross-linked using 5% ethylene glycol diglycidyl ether. The microspheres were subsequently rinsed and freeze-dried. Different pH of the coagulation media allows one to change the pore shape of CS microspheres. Microspheres from sodium alginate, sodium CMC, and sodium polyacrylic acid can be obtained from complex coacervation with CS. These microparticles originate via interatomic interaction between oppositely charged polymer solutions and KCl and CaCl2 solutions. First softened in the counter-ion solution, the resultant capsules were rinsed and dried.[62]

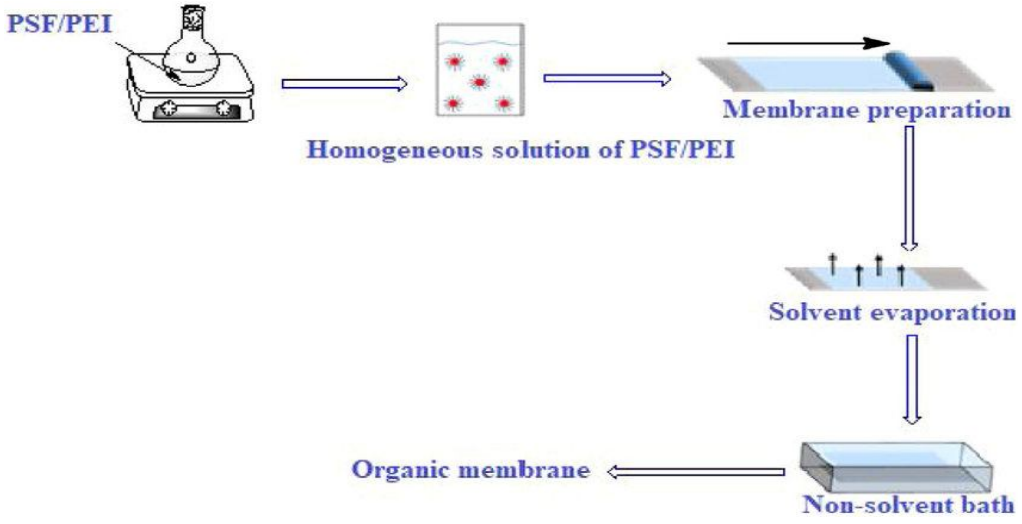

Fig.1.8 Wet Inversion Technique

1.8.3Hot Melt Microencapsulation:

Pellets of solid medicine that have been filtered down to less than 50 µm are added to the melted polymer after it has cooled. With the polymer suspended in a non-miscible solvent, such as silicone oil, the combination is heated to 5°C, just over its melting point, and agitated constantly. Cooling the emulsion till crystallisation of the polymer particles occurs occurs once it has stabilised. To clean the microspheres, petroleum ether is used for decantation. The primary motivation for creating this technology is to offer a microencapsulation process that works well with polymers that are sensitive to water, such as poly anhydrides. Microspheres can be made with diameters ranging from 1 to 1000 µm, and the size distribution can be easily controlled by changing the velocity of stirring. The sole drawback of this procedure is the relatively low temperature to which the medication is subjected.[62]

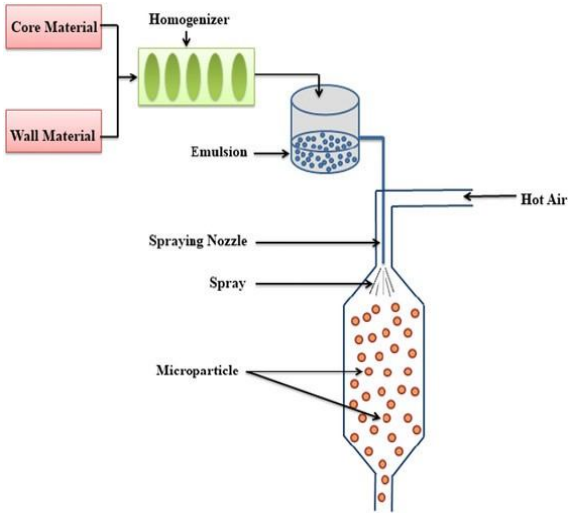

Fig.1.9 Hot Melt Microencapsulation

1.8.4 Single emulsion technique:

One can produce micro particle carriers made of natural polymers such proteins and carbohydrates by use of the single emulsion technique. First the natural polymers dissolve or disperse in an aqueous fluid; secondly they scatter in a non-aqueous media such oil. The scattered globule then is cross-linked using either chemical or heat cross-linkers such as glutaraldehyde, formaldehyde, or acid chloride.

Heat denaturation, however, is unsuitable for compounds with thermolabile character. Chemical cross-linking has the disadvantage of too much active component exposure to chemicals if applied at the time of preparation and subsequently subjected to centrifugation, washing, or separation.[62]

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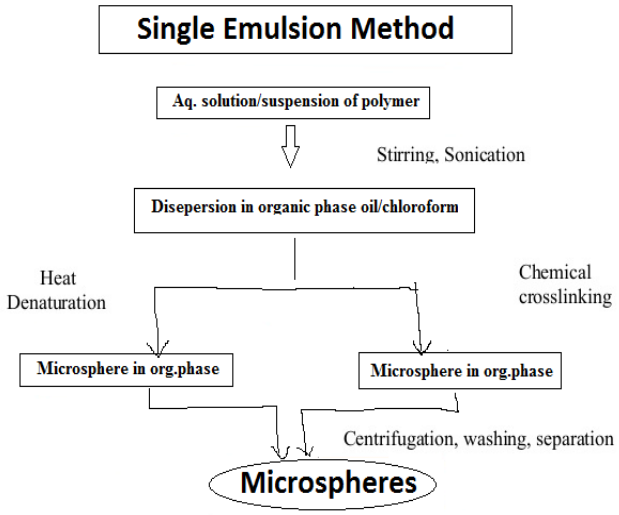

Fig.1.10 Single Emulsion Technique

1.8.5 Double emulsion technique:

Perfect for water-soluble medications, peptides, proteins, and vaccines, the double emulsion approach of microsphere development creates many emulsions either type w/o/w or another. One can use this method with synthetic and natural polymers.[62]

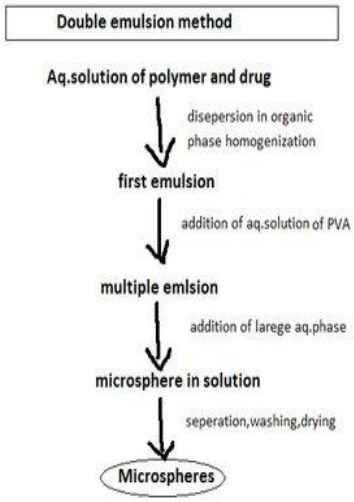

Fig.1.11 Double Emulsion Technique

1.8.6Polymerization techniques

Usually employed for the manufacturing of the microspheres, the polymerization methods fall mostly into two types:

I. Normal polymerization
II. Interfacial polymerization. Both are carried out in the liquid phase.

I. Normal polymerization

Micelle polymerizing, emulsion, bulk, precipitation, suspension, and other processes are all part of the polymerization process. The first step in bulk polymerization is to heat a monomer or mixture of monomers in the presence of a catalyst or initiator. The polymerization process allows for the loading of drugs, and the resulting polymer can be formed into microspheres. Bead or pearl polymerization, which involves heating a monomer or mixture of monomers that are dispersed as droplets in a continuous aqueous phase, is the process that allows for suspension polymerization. A variety of substances, including an initiator, could be contained in the drops.

Unlike suspension polymerization, emulsion polymerization results from the initiation diffusing to the surface of micelles in the aqueous phase.
Pure polymers can be produced using bulk polymerization, which is an advantage.

ll.Polymerization at interfaces

At the point where the two incompatible liquid phases meet, a large number of monomers react to produce a polymer film that essentially surrounds the dispersed phase.[62]

1.8.7<u>Phase separation coacervation technique</u>:

This approach is predicated on the idea of lowering the polymer's solubility in an organic phase to influence the coacervate generation in a phase rich of polymers. Under this approach, an incompatible polymer is introduced to the system and drug particles are distributed in a polymer solution, where the first polymer phases apart and absorbs the drug particles. Addition of a non-solvent causes the polymer to solidify. This technique has produced polylactic acid (PLA) microspheres utilizing butadiene as the incompatible polymer.[62]

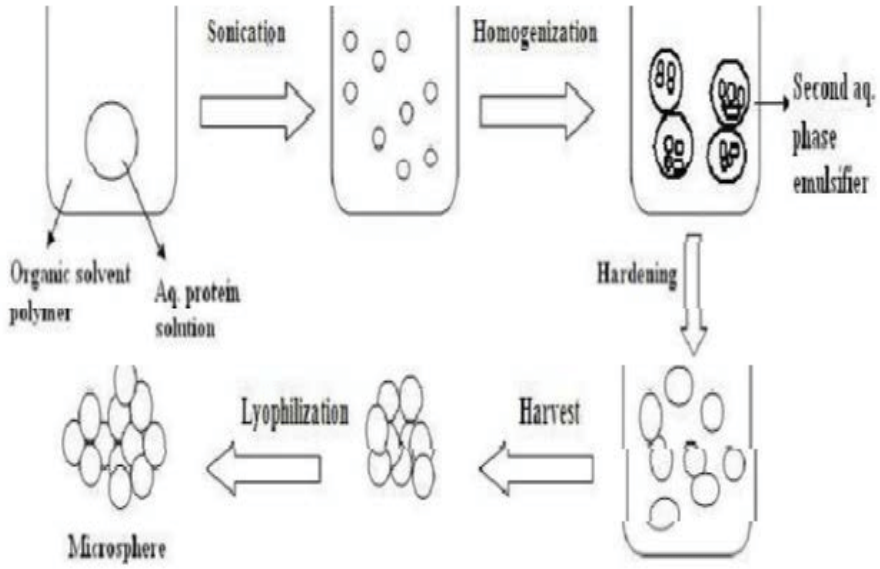

Fig.1.12 Phase separation technique

1.8.8Spray drying and spray congealing :

Using the approach of drying the mist the mixture generates, two techniques exist for producing microspheres from a polymer and a drug mixture.

The polymer is first broken down in an appropriate volatile organic solvent, such as dichloromethane or acetone, then combined. The drug's solid form then is distributed in the polymer solution by fast homogenization. After that, this mixture is atomized in a hot air stream to create fine mist or small droplets. The solvent evaporates very instantly to produce microspheres with a 1–100 µm size range. A cyclone separator separates the microparticles from the heated air; vacuum drying removes traces of solvent. The method offers one of the main benefits in that it can be carried out in aseptic circumstances. Many penicillin's are encapsulated by the spray drying technique.[62]

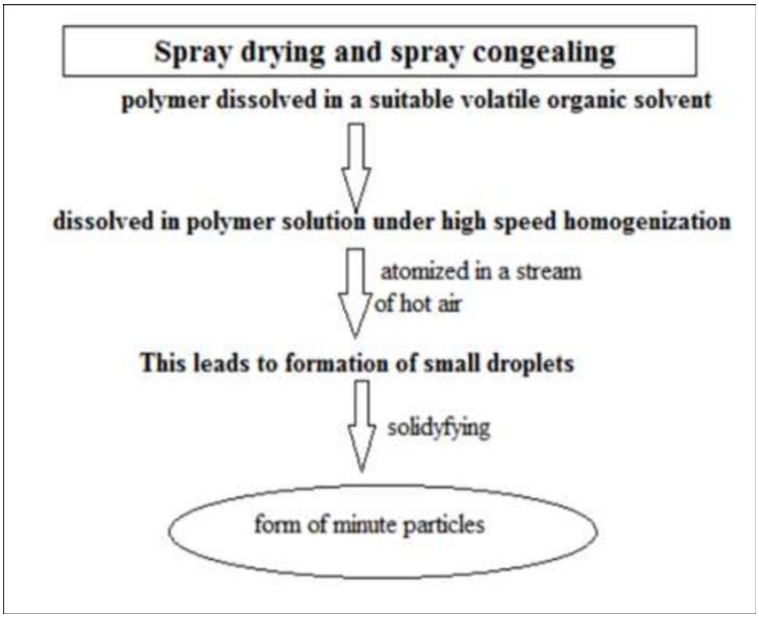

Fig.1.13 Spray drying technique

1.8.9 Solvent extraction

Microparticle preparation usually makes advantage of the solvent evaporation technique. This approach entails the extraction of the organic solvent thereby removing the organic phase. Usually used are water- miscible organic solvues like isopropanol. Extraction with water removes the organic component, therefore reducing the microsphere hardening time. One variant of the procedure entails the direct addition of the protein or medication to the polymer organic solution. Several elements affect the rate of solvent removal by extraction technique: water temperature, emulsion volume to water ratio, and polymer solubility profile.[62]

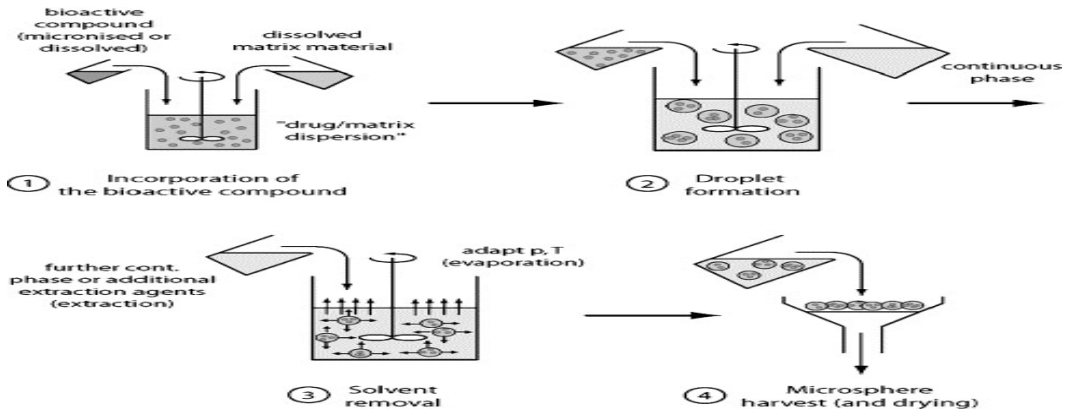

Fig.1.14 Solvent Extraction

1.9NEW MICROSOME DEVELOPMENTS

Important utilizations of chitosan polymer Cholesterol-lowering effects: Examples of fibers with high, moderate, and low bile acid-binding capabilities correspondingly were chitosan and cellulose. In this context, the processes behind cholestyramine's decrease of cholesterol were not stated.

1) Decreased cholesterol (food) intake,

2) Decreased cholesterol absorption efficiency, and

3) Increased fecal bile acid and cholesterol excretion.

Increase the stability of the drug: The medicine the drug is complexed with chitosan-made slurry and kneaded for 45 minutes till dough mass is more stable thanks to chitosan polymer. This quantity of dough passes through sieve number sixteen and produces fully stable grains under various situations.

Orthopedic patients: Natural polymer chitosan has been shown to have various useful characteristics including osteoconductive, improved wound healing, and antibacterial action. These characteristics make it frequently employed as a bioactive covering to increase the osseointegration of craniofacial and orthopedic implant devices. Effective in encouraging tissue growth for tissue repair and bone regeneration as well, chitosan has.

Dental Medicine:

Chitosan has been shown to accelerate wound healing, therefore improving the surface of the skin and preventing too strong scar development. In dental medicine it is also used as a tampon following aggressive treatment of maxillary sinusitis and as a bandage for oral mucous sores. It's also being investigated as a periodontal surgery absorbent membrane. Promoted as a nutritious meal that can be useful for treating and/or managing many diseases including arthritis, cancer, diabetes, hepatitis, and more, chitosan boasts a range of biological activity.

Chitosan as Permeation Enhancer: Chitosan's positive charge has been shown to be able to open tight connections in the cell membrane. This feature has spurred much research on the potential of chitosan as a permeation enhancer for hydrophilic medicines with perhaps low oral bioavailability, such peptides.

Chitosan as Mucoadhesive Excipient:

By improving their residence time in the gastrointestinal (GI) tract, bio adhesivity is a method used to raise medicine oral bioavailability. Comparatively to other cationic polymers like cellulose, xanthan gum, and starch, chitosan has been shown to have a better bio adhesivity.

Effect of chitosan: citric acid ratio on drug release :

It is shown that osmotic agents for the release of water-insoluble medicines can be polymers with suitable viscosity and expansion properties. Chitosan is low cost, totally biodegradable, toxicologically benign, and highly biassed by molecular weight and a linear unbranched form. Thus, it is clearly possible to use chitosan as a polymeric osmotic agent in osmotic pumps.

Chitosan as Permeation Enhancer:Cationic in character, chitosan has been found to open tight connections in a cell membrane. This feature has prompted various research on the use of chitosan as a permeation enhancer for hydrophilic medicines, which could otherwise have poor oral bioavailability, such peptides.

Enhanced bone formation by transforming growth factor (TGF-pl):To get high bone-forming efficacy, chitosan composite micro grains were made as bone substitutes.

Wound healing properties:initially noted in 1978, chitosan's effectiveness in promoting wound healing was initially Tough and protective, chitosan acetate films benefited from superior oxygen permeability, high water absorbability, and slow enzymatic breakdown.

1.10ULCERATIVE COLITIS

A long-lasting condition, ulcerative colitis causes inflammation and ulcers in the colon's and rectal's inner lining. Affecting the gastrointestinal tract, inflammatory bowel disease

(IBD) is a kind of chronic inflammatory disease. Crohn's disease is another sort of IBD. Usually absorbing water from stool, the colon loses its lining in UC, which produces symptoms including bleeding, pus generation, diarrhea, and stomach pain.

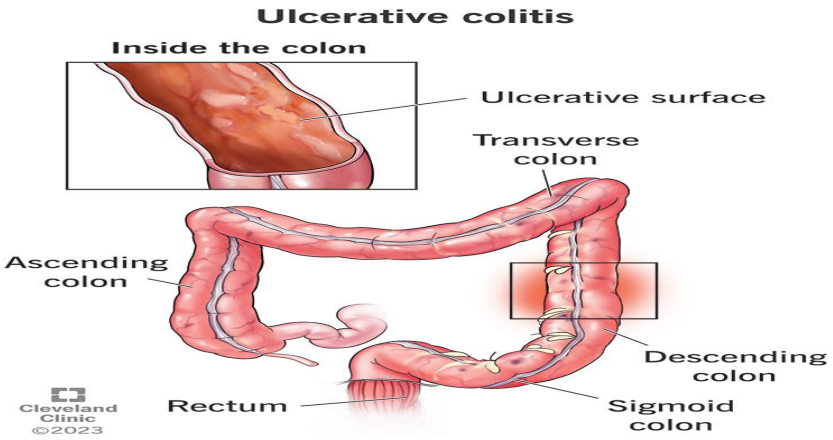

Fig.1.14 Ulcerative Colitis

Causes

Though there are various hypotheses, the reason of ulcerative colitis (UC) is yet unknown. Although those with UC have some immune system abnormalities, it is yet unknown if these issues are a cause or a result of the illness. By spotting and killing germs, viruses, and other possibly dangerous compounds, the immune system guards the human body from diseases. For those with UC, the immune system responds unusually to digestive tract microorganisms. UC may occasionally run in families, and some gene anomalies are more common in those with this disorder. Though sensitivity to some foods or items may not lead to UC, it can set off symptoms in some people. Although emotional pain does not lead to UC either, the stress of living with UC could aggravate the symptoms.

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Symptoms

The most often occurring UC symptoms include stomach pain and blood or pus in diarrhea. Additional symptoms include

- anemia
- fatigue
- fever
- nausea
- loss of appetite
- rectal bleeding
- loss of body fluids and nutrients
- skin lesions
- growth failure in children

Many people suffer with the disorder ulcerative colitis (UC). About 10% of UC sufferers have severe symptoms including recurrent fevers, bloody diarrhea, nausea, and severe stomach cramps, ranging from mild to severe. Apart from these symptoms, UC can also aggravate other conditions including kidney stones, liver illness, osteoporosis, eye discomfort, and joint pain. Fortunately, UC treatment helps many of these issues to be resolved.

Epidemiology and risk factors

Samuel Wilks originally detailed ulcerative colitis (UC) in 1859. Worldwide, UC is more often occurring than Crohn's disease (CD). It is more common in industrialized nations and has been rising in Asia. Second-generation South Asian immigrants to the United Kingdom (UK) had a greater prevalence of UC than the European population, according a prospective study from the country (17.2 versus 7 per 100,000 people annually). Reportedly, UC's general incidence and prevalence are 1.2–20.3 and 7.6–245 cases per 100,000 persons year, respectively.

UC has a bimodal age distribution; incidence peaks in the second or third decades of life and then follows a second peak between 50 and 80 years of age. Geographic differences have been noted in Europe and the USA; northern latitudes show more occurrence than southern latitudes. The following constitute UC's risk factors:

(1)**Age and gender**: Ulcerative colitis (UC) strikes persons in two different age groups since its bimodal age distribution. The second peak is seen between the ages of 50 and 80; the first incidence peak falls in the second or third decade of life. Though men and women have no consistent difference in UC rates, some research indicate that men are more likely to have the disorder.

(2) **Race and ethnicity**: IBD risk is three times higher for Jewish populations than for non-Jewish ones. Ashkenazi Jews predominate among the Jewish population over Sephardim, American, and European Jewish communities. Although initial studies indicated a significantly lower prevalence of IBD among African-American and Hispanic ethnicities when compared to the white populations, recent studies suggest that the difference in incidence between white and non-White populations is less than first believed, with same phenotypes.

(3) **Genetics**: More typically UC, between 8–14% of UC patients will have a family history of IBD. When compared to the non-Jewish population, the Jewish population shows more prevalence of UC. When compared with 1.6% among non-Jewish probands, the relative risk of UC development for first-degree relatives of a patient with UC is calculated to be 4.5%. Jewish probands The concordance rates in monozygotic twins are estimated at 16% and in dizygotic twins at 4%, according to twin studies.

(4) **Smoking**: Harries et al. initially documented the link between smoking and UC. Unlike CD, active smoking strongly inversely correlates with active UC (OR 0.58, 95% CI 0.45–0.75). The risk of UC rose in a prospective study two to five years after smoking cessation and stayed high for twenty years following.

(5) **Diet**: One theory holds that an immunological reaction to dietary antigens causes IBD to develop. Research show that a "Western" diet—which comprises processed meat, refined carbs, and other bad food choices—including processed meat, refined carbohydrates, and other unhealthy food choices—is connected to a higher risk of IBD.
(6) **Microbiota**: Several symptoms point to dysbiosis—that is, disturbance of the gut flora—in IBD. An changed composition of the commensal bacterial populations defines dysbiosis and causes dysregulation of the immune response to bacterial antigens. In CD more than in UC, this variation in microbial diversity is more important.
(7) **Appendectomy**: Appendectomy affects UC and CD differently, much like smoking does. A past appendectomy was linked in patients with UC to clinically milder disease, lower relapse rates, and less need for immunosuppressive; it had no evident impact on the likelihood of colectomy.

Diagnosis of ulcerative colitis:

Clinically presented, endoscopic results, histology, and ruling out other possible diagnosis all help determine ulcerative colitis (UC). Dietary deficits are screened for and nutritional state is assessed using serum albumin levels, iron tests, and vitamin B12 levels. A sign of serious illness, hypoalbuminemia also predicts poor response to medical treatment and colectomy.[23]

Differentiating UC from Crohn's disease (CD) using serology testing Perinuclear anti-neuronal anti-neutrophil cytoplasmic antibodies (p-ANCA) and anti-Saccharomyces cerevisiae antibodies (ASCA) are the two most often measured antibodies. Whereas in UC the associated pattern is ASCA-/p-ANCA+, in CD the usual pattern is ASCA+/p-ANCA-, By serology, histology, culture, or DNA PCR testing, patients with severe, refractory illness should be assessed for CMV infection.[23]

In UC patients, stool investigations including lactoferrin levels and fecal calprotectin (neurrophil-derived biomarker) help to evaluate the degree of inflammation and identify clinical recurrence. Especially for those who recently visited endemic locations, microscopy for ova and parasites (three tests) and a Giardia stool antigen test should also be done.([23)

When talking about the restrictions of present therapy choices for ulcerative colitis, it's crucial to cover both systemic adverse effects and the difficulty of properly focusing the diseased colon.

(a) **Systemic Side Effects**: Many conventional ulcerative colitis treatments including corticosteroids, immunosuppressants, and biologic therapy can cause systemic adverse effects. These adverse effects can include:

- Because of their effects on the immune system, immunosuppressive medications raise a risk of infections.
- Osteoporosis: Corticosteroid use over lengthy periods of time could cause bone loss and higher fracture risk.
- Some drugs aggravate ulcerative colitis sufferers by causing diarrhea, nausea, or vomiting.

- Corticosteroids and immunosuppressants may cause acne, skin thinning, or other dermatological problems.
- Long-term immunosuppressive medication use may raise the risk of several malignancies.

(b) **Inadequate Targeting of the Inflamed Colon**:

- Conventional oral drugs are sometimes given systemically, which results in non-specific distribution all across the body and could so lower their efficacy.
- Oral drugs may take time to reach therapeutic concentrations at the colon's site of inflammation, therefore postponing symptom alleviation.
- Restricted bioavailability: Oral medicines' bioavailability can be lowered by first-pass metabolism and gastrointestinal tract degradation; so, greater doses are required and systemic side effects risk increases.
- With standard oral formulations, maintaining therapeutic drug levels in the inflamed colon over an extended period might be difficult and cause oscillations in symptom management and disease relapse.[23]

Improving ulcerative colitis treatment's safety and efficacy depends on addressing these constraints. By improving drug localization to the inflamed colon and therefore reducing systemic exposure and related side effects, developing targeted drug delivery systems like microspheres containing Boswellia serrata and Aloe vera gives the possibility to overcome these problems.

CHAPTER-2

LITERATURE REVIEW

Nikita, et al.,Dec 2023): "Extraction, identification, analytical method developmentand Validation of boswellic acid using UV spectrophotometric method". The UV Spectroscopic method for analysis of Boswellic acid was in accordance with ICHQ2 (R1) guidelines and it satisfies acceptance standards. The analytical approach was foundto be specific, precise, linear, accurate, robust, and can be used for assay of boswellic acidas bulk drug and pharmaceutical dosage formulations containing boswellic acid. Thecurrent analytical technique is suitable for the intended applications.

Parul, et al., (March 2023): "Formulation and Development of Boswellia serrata Extract-Loaded Microspheres for Targeted Delivery of Anti-Inflammatory Agents" Microspheres were made using PLGA and B. serrata extract dissolved in dichloromethane, then emulsified with polyvinyl alcohol as a surfactant in an aqueous phase. On the basis of encapsulation efficiency and drug loading, the ratio between PLGA and B. serrata extract was optimized.

Shraddha Prashant,et al.,(Dec 2022): "A review on microsphere for novel drug delivery system"Microspheres are an advanced approach to the drug delivery in an innovative way. They have better patient compliance and targeted precision compared to the other forms of drug delivery systems and are safer for medication delivery. Due to its benefits of continuous and controlled-release action, improved stability, decreased dosing frequency, dissolving rate and bioavailability, microspheres are the most popular drug delivery technology.

Dana, et al., (Sept 2022): "Curcumin-Loaded Microspheres Are Effective in Preventing Oxidative Stress and Intestinal Inflammatory Abnormalities in Experimental Ulcerative Colitis in Rats". In the present study, a novel curcumin-loaded polymeric microparticulate oral-drug delivery system (Col-CUR-MPs) for colon targeting was administered in order to evaluate whether this system could be used for the prevention of AA-induced colitis. Compared to non-encapsulated curcumin, the curcumin-loaded microparticulate system demonstrated a much higher antioxidant and anti-inflammatory activity, presenting the most elevated levels of CAT and TAC, a lower oxidative stress for most of the determined parameters (NOx, TOS, OSI), and a significantly lower amount of tissue damage.

Devkar, et al., (June 2022): "Extraction, Formulation and Evaluation of Boswellia Serrata containing ointment for management of Inflammation" The present study revealed that the optimized herbal formulation F2 consisting of Boswellia serrata extract shows comparatively. FT-IR study revealed that the reisno possible drug interaction with other component present in extract and DSC study depicts the presence of boswelic acid in the extract .

Hamdi Nsairat,et al.,(May 2022): "Liposomes: structure, composition, types, and clinical applications" Liposomes were successfully utilized as an efficient drug delivery system for various diseases ranging from cancer treatment to pain managing. The biocompatible, biodegradable, and low immunogenicity liposomes formulation enhanced the pharmacokinetics and pharmacodynamics properties of water insoluble, poor bioavailable and highly toxic drug. Liposomes undergone numerous evolutions in terms of their constituents and manufacturing process to overcome their early limitations.

Pranali, et al., (Feb 2022): "Recent Trends in Novel Drug Delivery System" Novel Drug delivery System (NDDS) NDDS can be a mixture of improve method and new indefinite quantity forms that area unit a great deal better than preferred dosage forms. Advantages of Novel Drug Delivery System are: Optimum dose at the best time and proper location, affordable use of expensive drugs, excipients and discount in cost, useful to patients, better clinical aid, stepped forward consolation and commonplace of living

Puneet, et al., (August 2021): "An Overview on "Boswellia serrata" The present literature review provides the path to understanding the various pharmacotherapeutic properties of B. serrata, an ancient medicinal plant. After a detailed literature review, it was noteworthy that the plant's activities mentioned by classical literature were found when it was investigated through the latest pharmacological tools and subjected to preclinical studies. Hence, the present review gives the path to future clinical research and active phytoconstituents in the plant.

Mousami, et al., (April 2021): "A REVIEW ON MICROSPHERES AS A NOVEL CONTROLLED DRUG DELIVERY SYSTEM" Microspheres are a type of novel drug delivery system where the drug is enclosed in spherical shaped structures which are made up of different polymers forming a matrix system. The drug liberates out of the microspheres by slow release through the matrix system.

Roshan, et al., (Jan 2021): "A REVIEW ON NOVEL DRUG DELIVERY SYSTEM" Nanoparticles are a promising controlled and selective release mechanism for drug delivery. The advancement of nanotechnology would undoubtedly have important consequences for the drug supply industry, affecting virtually every route from oral to injectable. And lower drug toxicity, lower cost of treatment, greater bio-availability and expanding the economic life of patented medicines are projected to pay for both physicians and patients.

Sudhanshu, et al., (Sept 2020): "Boswellia serrata Roxb.– A Bioactive herb with various pharmacological activities"BA has gained widespread exposure for its various health advantages which mainly tend to work through anti-inflammatory mechanism. They are also used as expectorant, antiseptic, and antineurotic drug. Alcohol extract from frankincense inhibit the growth of bacteria as well as fungi. Boswellia preparation like topical preparation inhibits 5-LO and prevents the formation of leukotrienes.

Sunil, et al., (Nov 2020): "Formulation and Evaluation of Microsphere of Aceclofenac" Solvent evaporation technique has been successfully employed to produce Aceclofenac loaded ethyl cellulose and Eudragit microspheres with optimal drug encapsulation that sustained the drug release over a period of time (Figure 1). The formulation variable drug – polymers and polymers – polymers ratio exerted a significant influence on the drug encapsulation. The present study signifies the utility of microspheres in retarding the drug release. This may in turn reduce the frequency of dosing, thereby improving the patient compliance.

Pallavi, et al., (April 2020): "In-vitro anthelmintic activity of Boswellia serrata and Aloe barbadensis extracts on Pheretima posthuma: Indian earthworm".In conclusion, the present study proves the potential of the combination of B. serrata and A. barbadensis as an anthelmintic drug. Further studies are necessary to isolate and reveal the active compounds and to establish the mechanism of action.

Abrar Anam, et al., (March-April 2020): "Formulation and evaluation of microsphere of antiulcer drug using Acacia nilotica gum". Natural polymer A. nilotica gum was successfully used for the preparation of famotidine microparticulates. Formulation with A. nilotica gum was impacted to the particular size, surface morphology, swelling conduct, and in vitro drug release. Stability studies F1, F3, and F5 formulations showed no reduction in drug content and in percent release. A. nilotica gum may be utilized during pharmaceutical dose frames by giving support to drug delivery system and avoiding side effects for the" patients.

Mahesh Gajendra, et al., (Dec 2019): "A comprehensive review and update on ulcerative colitis" In summary, it is difficult to predict the prognosis of patients with UC. It is necessary to individualize each patients' assessment and treatment plan in order to produce the best health outcomes. Not one approach is a perfect fit for every patient and one patient may require multiple treatment modalities to achieve remission.

Manohar D, et al.,(July 2019): "A Review on Microsphere and its application" Microspheres are multiparticulate drug delivery systems which are prepared to obtain prolonged or controlled drug delivery to improve bioavailability, stability and to target the drug to specific site at a predetermined rate. They are made from polymeric waxy or other protective materials such as natural, semi synthetic and synthetic polymers. Microspheres are characteristically free flowing powders having particle size ranging from 1–1000 μm consisting of proteins or synthetic polymers.

Mitsuro Chiba, et al., (April 2019): "Relapse Prevention by Plant-Based Diet Incorporated into Induction Therapy for Ulcerative Colitis: A Single-Group Trial" The cumulative relapse rates at 1 and 5 years in the initial episode cases after induction therapy incorporating PBD were 14% and 27%, respectively. The PBDS was significantly higher than baseline even at 6-year follow-up. The relapse rates were lower than those previously reported with conventional therapy in Europe. This difference is consistent with our hypothesis that this PBD prevents relapse of UC.

Nameeta, et al., (April 2019): "An Update on pharmacological profile of Boswellia serrata" The present review focuses on the scientific recognition of the remedial usefulness and action of B. serrata once used in cultural and religious ceremonies but now valued for its numerous beneficial medicinal effects. BAs are the bioactive phytoconstituents which have demonstrated promising results in numerous experiments and clinical studies.

Priyanka, et al., (August 2018): "Formulation development of acyclovir microsphere using novel natural polymer" It was concluded from this study that the microsphere can be prepared from kondagogu gum by emulsifying solvent evaporation method and can be loaded with the drug acyclovir for its sustained delivery in the GIT system. The prepared microspheres were optimized for different formulations and process variable concentrations and found that the microsphere was uniform and acceptable size range. V.N.L. Sirisha, et al., (August 2017): "Formulation and Evaluation of Karaya gum Microspheres of Cromolyn sodium- Treatment of Ulcerative Colitis."

Karaya gum microspheres were capable of targeting the release of cromolyn sodium (mast cell stabilizer) in colon for the management of colitis in both the methods. The release was retarded until it reaches the large intestine by both the methods. It was concluded from the study that karaya gum can be successfully used for colon targeted drug delivery on a daily dosage form.

Qiang- Song Wang, et al., (Dec 2016): Colon targeted oral drug delivery system based on alginate-chitosan microspheres loaded with icariin in the treatment of ulcerative colitis. The targeted microspheres loaded with icariin could decrease the colon mucosa damage index by reducing the productions and gene expressions of inflammatory mediators and cytokines. The microspheres cross-linked by glutaraldehyde could increase the residence of drugs in the colon and avoid drug loss in the upper and middle regions of digestive system.

Rameshwar Deshmukh,et al., (Sep 2016): "Solvent evaporation and spray drying technique for micro- and nanospheres/particles preparation: A review This article presents a comprehensive review of research relating to the preparation of biodegradable and biocompatible controlled/sustained release of micro and nanoparticles. It covers recent developments in the area of technology through solvent evaporation followed by lyophilization and spray drying.

Deepak, et al., (June 2016): "Microsphere a review"icrospheres received much attention not only for prolonged release, but also targeting of anticancer drugs. In future by combining various other strategies, microspheres will find the central place in novel drug delivery, particularly in diseased cell sorting, diagnostics, gene and genetic materials, safe, targeted and effective in vivo delivery and supplements as miniature versions of diseased organ and tissues in the body.

Kapil, et al., (October 2012): "Development and Evaluation of Floating Microspheres of Curcumin"Curcumin floating microspheres were successfully developed using emulsion solvent diffusion method. The microspheres had good yield and showed high, drug entrapment efficiency. The flow properties of microspheres were within the acceptable range and therefore would be easily filled into capsules.

Suresh, et al., (Jan-Mar 2011): "Formulation and Evaluation of Floating Microspheres of Boswellic acid"In vitro data obtained for floating microspheres of Boswellic acid showed excellent buoyancy, good Entrapment Efficiency and prolonged drug release. Microspheres of different size and drug content could be obtained by varying the formulation variables. Diffusion was found to be the main release mechanism.

Praveen K. Yadav, et al., (March 2009): "Current Strategies for the Treatment of Ulcerative Colitis"Several types of medications are used to control inflammation or reduce symptoms caused by UC. Mesalamine is useful to achieve and maintain remission. Some patients may need corticosteroids (e.g., prednisone) to control inflammation and induce remission.

Immunosuppressives (6-MP and AZA) are very effective. Infliximab finds TNF in bloodstream and removes it before it causes inflammation in intestinal tract. Ileal-anal pouch surgery is the most common surgery for UC. Proctocolectomy surgery also involves removing the colon and rectum, which eliminates ulcerative colitis.

CHAPTER- 3

AIM AND OBJECTIVES

3. AIM & OBJECTIVES

Usually, the goals and aims of developing and accessing Aloe vera and Boswellia serrata for ulcerative colitis treatment for a thesis project comprise several important components:

1. Aim:

• The major purpose of the research, which is to find out whether Boswellia serrata and Aloe vera can help with ulcerative colitis.

2. Objectives:

- Review the body of knowledge already in publication on ulcerative colitis, including pathogenesis, present treatment choices, and any past research on the use of Aloe vera and Boswellia serrata in this setting.
- Either alone or in combination, develop formulations (e.g., extracts, formulations for oral administration) including Boswellia serrata and Aloe vera fit for the treatment of ulcerative colitis.
- Characterize the developed items in order to evaluate their physicochemical qualities, stability, and compatibility.
- In vitro studies will let you assess the formulations' anti-inflammatory effectiveness, antioxidant qualities, and any other pertinent ulcerative colitis treatment-related parameter value.

3. Outcome:

- The thesis should end with a synopsis of the results, debating the safety and efficacy of the developed products relative to conventional treatments and offering understanding of their possible modes of action.
- If relevant, recommendations for next study paths and clinical trials could also be added.

By addressing these aim and objectives, Further research and clinical applications in the field of ulcerative colitis may be possible with the useful insights provided by the thesis regarding the potential usage of Boswellia serrata and Aloe vera.

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CHAPTER- 4

PLAN OF WORK

4. PLAN OF WORK

Keeping the objectives of the study in mind, the following plan of work followed

1. RESEARCH PHASE

Literature Review: Gather information on Boswellia serrata, Aloe vera, microspheres, and ulcerative colitis.

Identify Key Components: Determine the active compounds in Boswellia serrata and Aloe vera relevant to ulcerative colitis treatment.

Formulation Design: Decide on the formulation strategy for microspheres (e.g., encapsulation techniques, excipients).

2. PREPARATION PHASE

Material Collection: Procure Boswellia serrata extract, Aloe vera extract, and microsphere formulation materials.

API collected from Bacfo Herbal Pharmaceutical from Noida

Laboratory Setup: Arrange necessary equipment and facilities for formulation preparation.

3. FORMULATION PHASE

Microsphere Preparation: Formulate Boswellia serrata and Aloe vera microspheres.

Optimization: Experiment with different formulations to optimize drug loading, particle size, and release characteristics.

4. CHARACTERIZATION

Physical Characterization: Assess microsphere morphology, size distribution, and surface characteristics using techniques like SEM (Scanning Electron Microscopy).

Chemical Analysis: Determine drug encapsulation efficiency, drug release kinetics, and stability under various conditions.

5. DATA ANALYSIS

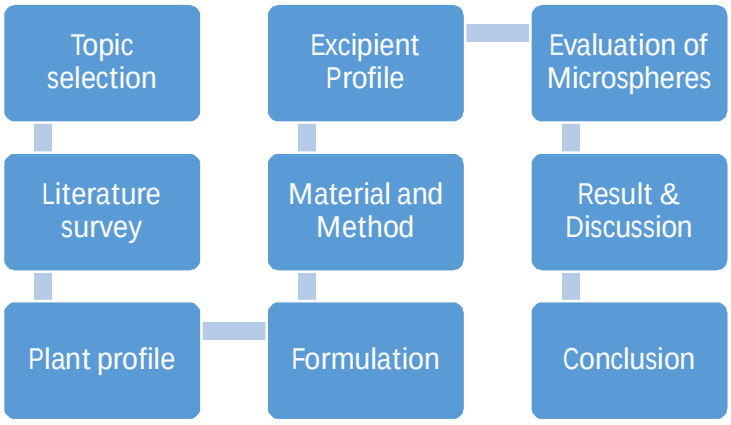
Statistical Analysis: Analyze experimental data using appropriate statistical methods to draw conclusions.

Interpretation: Interpret results in the context of the research objectives and existing literature.

6.DOCUMENTATION AND REPORTING

Thesis Writing: Compile findings, discussions, and conclusions into a cohesive thesis document.

Presentation: Prepare presentations summarizing the research for academic or professional audience.



CHAPTER-5

DRUGS AND EXCIPIENT PROFILE

5. DRUGS & EXCIPIENTS

5.1 BOSWELLIA SERRATA:

Commonly known as "Salai guggal," "Shallaki," "gugu," and "kundur," Boswellia serrata is a medium-height shrub with a circumference between 1.2 and 3 m. It members the "Burseraceae" family.

Often utilized in traditional medicine for their anti-inflammatory effects is the shrub Boswellia serrata. Boswellia serrata's strong anti-inflammatory action has made it a desirable target for the creation of anti-inflammatory medications. Microspheres allow Boswellia serrata extract to be more bioavailable, less adverse effects, and more effective to be encapsulated. This work will help to create new antiinflammatory medications and offer fresh understanding on the possibilities of Boswellia serrata extract-loaded microspheres for the treatment of inflammatory diseases. The work intends to maximize the formulation process to generate microspheres with sustained release characteristics and high drug loading efficiency.

Fig.5.1 Boswellia serrata

Boswellic acid has several pharmacological effects, including respiratory problems (cough, cold, asthma, bronchitis, dyspnea, and hoarseness) and the conventional treatment for GI illnesses (vomiting, diarrhea, constipation, and flatulence). All these pharmacological activities are ascribed to boswellic acid from exudates of the Boswellia plant, hence extraction and purification of boswellic acid from Boswellia plant exudate is absolutely necessary.

Here's a drug profile of Boswellia serrata:

Name: Boswellia serrata

Common Name: Indian frankincense, Salai guggul

Family: Burseraceae

Traditional Uses:

1. Boswellia serrata has long been used to help with inflammation, especially in disorders including inflammatory bowel illnesses and arthritis.
2. Often used to reduce osteoarthritis and rheumatoid arthritis symptoms, anti-arthritic is
3. Arthritis, back discomfort, and sports injuries are among the several disorders for which it helps with pain relief.
4. Boswellia serrata has long been used to improve digestive health, particularly the treatment of symptoms linked with ulcerative colitis and Crohn's disease.
5. Respiratory Health: Among traditional applications are bronchitis and asthma symptom relief.

Active Ingredients:

1. Boswellic acids are thought to be the main active molecules for Boswellia serrata to have therapeutic effects. They are anti-arthritic and anti-inflammatory.

.

Pharmacological Actions:

1. Boswellic acids cut inflammation by blocking pro-inflammatory enzymes including leukotrienes and 5-lipoxygenase.
2. Boswellia serrata could help with arthritis by lowering inflammation and stopping cartilage loss.
3. Analgesic: It helps in disorders related to pain and inflammation since it contains qualities to reduce discomfort.
4. Boswellia serrata might change the immune response, hence dosage helps to explain its anti-inflammatory action.

DosageForms: Boswellia serrata is available in various forms, including:

- Capsules: Standardized extracts containing specific amounts of boswellic acids.
- Tablets: Formulated with Boswellia serrata extracts.
- Topical Creams or Gels: For local application to areas of pain or inflammation.

Dosage: Formulation and the particular condition being treated will affect dosage. Usually split into several doses, dosages range from 300 mg to 1200 mg daily. Still, it's imperative to do as advised by the manufacturer or healthcare professional.

Adverse Effects: Boswellia serrata is generally well-tolerated when used at recommended doses. However, some individuals may experience:

- Gastrointestinal Disturbances: Including nausea, diarrhea, or acid reflux.
- Allergic Reactions: Rarely, some individuals may experience allergic reactions to Boswellia serrata.

Drug Interactions:

- Boswellia serrata can interact with some drugs, particularly those metabolised by the liver or those with anti-inflammatory action. Before using Boswellia serrata supplements, particularly if you already take other drugs, you should see a healthcare practitioner..

Contraindications:

- There are no absolute contraindications for Boswellia serrata, but individuals with known allergies to Boswellia serrata or its components should avoid its use.

Pregnancy and Lactation:

- There is limited information available regarding the safety of Boswellia serrata during pregnancy and lactation. Pregnant and breastfeeding women should consult with a healthcare professional before using Boswellia serrata supplements.

Regulatory Status:

- In many countries, Boswellia serrata supplements are sold as dietary supplements and are not regulated as strictly as pharmaceutical drugs. It's essential to choose products from reputable manufacturers to ensure quality and safety.

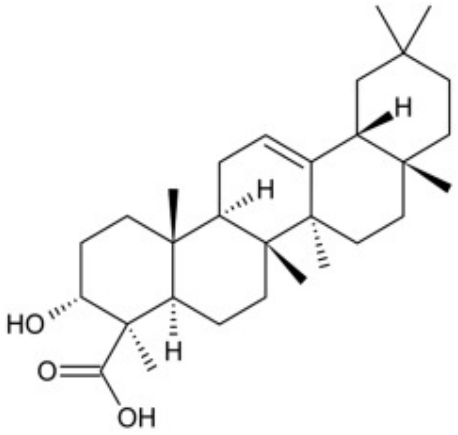


Fig. 5.2 Chemical structure ofBoswellia serrata

5.2 ALOE VERA:

Members of the Liliaceae family, aloe vera is a perennial succulent or xerophyte with either very short or nonexistent stems. Its elongated, pointed leaves store a lot of water, and their tissue is what Although Aloe vera (L.) Burm.f. (Aloe barbadensis Miller) belongs to the Asphodelaceae family and has over 500 Aloe species, A. barbadensis and A. arborescens are the two most often grown commercially worldwide and used for different medical, cosmetic, and nutraceutical applications. Before being harvested to be

used for aloe product manufacture, aloe leaves need roughly 4 years to achieve maturity and have a lifetime span of roughly 12 years. The leaf comprises mostly an interior pulp or mucilaginous gel and an exterior green rind (skin). The leaf lining at the junction between the rind and the inner pulp features a vascular bundle.

Fig.5.3 Aloe vera

After sterilization, filtering, decolorization (activated charcoal absorption), sterilization, concentration, and dehydration the obtained juice is Though the outer rind is first removed, the inner leaf juice is produced similarly to whole leaf juice in terms of method.

.

Classification:

Aloe vera is classified as a botanical drug or a natural remedy due to its therapeutic properties.

Therapeutic Class: Aloe vera is primarily used as an herbal remedy, falling under various therapeutic classes such as:

- Dermatological agents: For treating various skin conditions like burns, wounds, eczema, and psoriasis.
- Gastrointestinal agents: Used for digestive issues including constipation, indigestion, and irritable bowel syndrome (IBS).
- Anti-inflammatory agents: Aloe vera contains compounds that exhibit anti-inflammatory properties, which can help in reducing inflammationand pain**.**

Mechanism of Action: Aloe vera contains several bioactive compounds including polysaccharides, glycoproteins, enzymes, vitamins, and minerals. These compounds are believed to contribute to its therapeutic effects. For example:

- Polysaccharides stimulate the immune system and promote wound healing.
    - Glycoproteins have anti-inflammatory properties and help in reducing pain and inflammation.
    - Enzymes like bradykinase aid in the breakdown of dead tissue, promoting wound healing.

- Vitamins and minerals provide nourishment to the skin and body, aiding in overall health and healing processes.

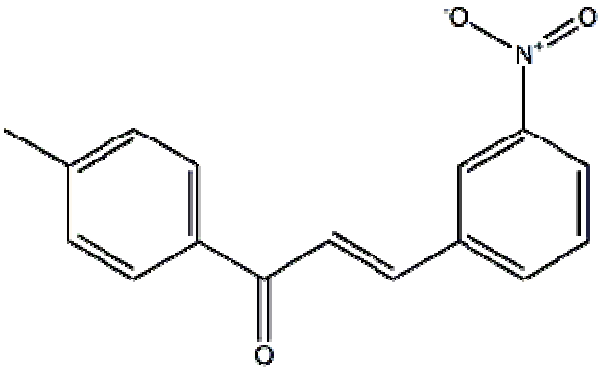


Fig. 5.3 chemical structure ofaloe vera

Indications: Aloe vera is used for various medical and cosmetic purposes, including:

- Topical application for burns, cuts, wounds, sunburns, frostbite, psoriasis, and eczema.
- Oral consumption for gastrointestinal issues such as constipation, indigestion, and IBS.
- Cosmetic use in skin care products for moisturizing, soothing, and anti-aging effects.

Dosage Forms: Aloe vera is available in various forms including:

- Topical gels, creams, lotions, and ointments for external application.
- Juices, capsules, tablets, and powders for oral consumption**.**

Adverse Effects: While aloe vera is generally considered safe when used topically or orally in appropriate doses, some individuals may experience adverse effects such as:

- Topical application may cause skin irritation or allergic reactions in some people.
- Oral consumption of aloe latex (derived from the inner leaf) may lead to gastrointestinal discomfort, cramps, diarrhea, and electrolyte imbalances if taken in excess.

Contraindications: Aloe vera should be used with caution or avoided in certain situations:

- Pregnancy and breastfeeding: Oral consumption of aloe vera is not recommended during pregnancy and breastfeeding due to potential risks.
- Allergy: Individuals with known allergies to plants in the Liliaceae family (e.g., onions, garlic) may be allergic to aloe vera.

- Medical conditions: People with certain medical conditions such as diabetes, intestinal disorders, or electrolyte imbalances should consult a healthcare professional before using aloe vera**.**

Drug Interactions: Aloe vera may interact with certain medications, including:

- Digoxin: Aloe vera may decrease the absorption of digoxin, reducing its effectiveness.
- Diuretics: Aloe vera may enhance the effects of diuretic medications, leading to electrolyte imbalances.
- Sevoflurane: Aloe vera may increase the risk of hypokalemia (low potassium levels) when used with sevoflurane anesthesia**.**

Monitoring Parameters: Aloe vera users should be watched for any side effects, particularly if taken orally or for prolonged lengths of time. Monitoring criteria could include for gastrointestinal problems, skin irritation, electrolyte balance, and drug interactions.

Particularly in dermatology and gastrointestinal health, aloe vera is a flexible plant cure with several therapeutic uses. Although aloe vera products are generally regarded as safe, especially in people with pre-existing medical disorders or those on drugs, one should use them sensibly under the direction of a healthcare practitioner.

EXCIPIENTS PROFILE:

5.3 HYDROXYPROPYL METHYLCELLULOSE-

Commonly employed in pharmaceuticals, hydrophilic polymer HPMC is affordable, safe, effective, and readily available. Among its several uses—controlled release, dry coating, film coating, direct compression, flow property, swelling, etc.—HPMC has been studied in terms of number of applications.

With an empirical formula C8H15O8-(C10H18O6)n-C8H15O8 and a molecular weight roughly 86000, hydroxypropyl methylcellulose This product consists of a semisynthetic mixture of hydroxypropyl ether and methylcellulose. White or creamy-white fibrous or granular powder, hpmc is odorless and tasteless. It has a specified viscosity colloidal solution and can be dissolved in water to form a translucent to milky white. The several grades of HPMC are obtained from variations in the content of the Methoxy and Hydroxyl substitution.

Applied in colon-targeted formulation, HPMC has good gastric protective qualities.

TABLE 5.1-Chemistry of HPMC

Parameters	**Specifications**
Molecular formula	$C_{56}H_{108}O_{30}$
Molecular Weight	1261.4 g/mol
Solubility	Soluble in cold water, 70% ethanol, practically insoluble in hot water
Melting point	190C-200□C
Stability	Stable in acid and alkali, the Aqueous solution of HPMC is enzyme, resistant in nature, it is stable between pH 3-11 during long-term storage
Incompatibility	It is incompatible with an oxidizing agent.

5.4 ETHYLCELLULOSE-

Ethyl cellulose, sometimes known as ethyl cellulose, is a variation of cellulose whereby some of the hydroxyl groups on the repeating glucose units are transformed into ethyl ether groups. Manufacturer will affect the number of ethyl groups.

Investigated as a hydrophobic sustained release carrier with anti-oxidation effect is ethyl cellulose. The microsphere wall thickness and surface area define the release of medication from high-viscosity ethyl cellulose.

Mostly employed as thickeners in cosmetics and industrial operations, it is a thin-film coating material for covering paper, vitamins, and medical pills.

Commonly used as a coating material for pills and capsules, ethyl cellulose offers a protective layer that keeps the active chemicals from being released too rapidly in the digestive tract. In a range of food, cosmetic, and medicinal goods, EC also finds usage as a binder, thickener, and stabilizer.

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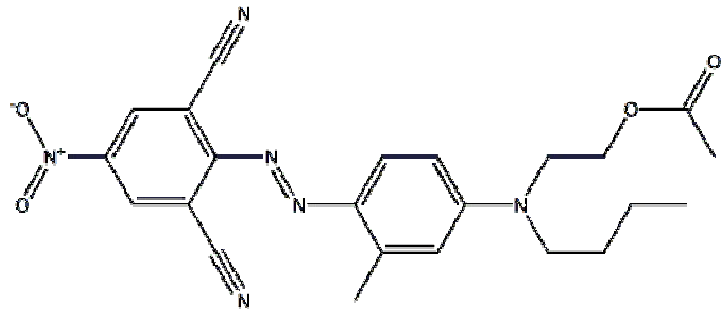


Fig.5.4 Ethyl Cellulose

Melting point	240-255 °C
Density	1.14 g/mL at 25 °C (lit.)
Refractive index	*n*20/D 1.47(lit.)
Storage temp.	2-8°C
Solubility	esters, aromatic hydrocarbons, alcohols and ketones: soluble
Form	Powder
Specific Gravity	1.14
Color	White to slightly yellow
Viscosity	18-22 cps
Water Solubility	Insoluble

5.5 GLYCEROL:

Widely used in food, personal care, and pharmaceuticals, glycerol—also called glycerin or glycerin—is a colorless, odorless viscous liquid. In drugs, it has several purposes and is frequently used as an excipient. Glycerol as an excipient has a profile here:

1. Chemical Structure:

- Glycerol is a trihydric alcohol (polyol) with the chemical formula C3H8O3.
- It consists of a propane molecule with three hydroxyl (OH) groups attached, which makes it highly hydrophilic (water-loving).

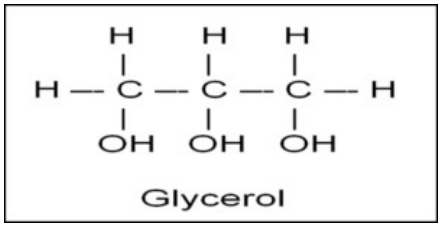


Fig.5.5 Glycerol

2. Solvent Properties:

- Glycerol is miscible with water and many organic solvents, making it an excellent solvent or co-solvent in pharmaceutical formulations.
- It can be used to dissolve both polar and non-polar substances, enhancing the solubility of active pharmaceutical ingredients (APIs) in formulations**.**

3. Humectant and Moisturizing Properties:

- Glycerol is hygroscopic, meaning it attracts and retains moisture from the air.
- In pharmaceuticals, it is commonly used to prevent formulations from drying out and to maintain their moisture content.
- It is also utilized in topical preparations such as creams, lotions, and ointments to provide moisturizing effects.

4. Lubricating Properties:

- Glycerol's viscous nature makes it an effective lubricant, improving the flow properties of formulations during manufacturing processes.
- It is often added to oral dosage forms such as syrups and suspensions to improve swallowability and mouthfeel.

5. Plasticizing Agent:

- Glycerol is used as a plasticizer in the production of suppositories, soft gelatin capsules, and other solid dosage forms.
- It helps to impart flexibility and elasticity to these formulations, making them easier to handle and administer.

6. Stability Enhancer:

- Glycerol can enhance the stability of certain pharmaceutical formulations by reducing crystallization, preventing the precipitation of salts, and inhibiting microbial growth.
- It is often included in liquid and semi-solid formulations to extend their shelf life.

7. Compatibility:

- Glycerol is generally compatible with a wide range of other excipients and APIs commonly used in pharmaceutical formulations.
- However, its hygroscopic nature may affect the stability or physical properties of certain compounds, so compatibility testing is advisable**.**

8. Safety and Regulatory Status:

- Glycerol is considered safe for use in pharmaceuticals when used within specified concentrations and in accordance with regulatory guidelines.
- It is approved by regulatory agencies such as the FDA (Food and Drug Administration) in the United States and the EMA (European Medicines Agency) in the European Union for use as an excipient in pharmaceutical formulations.

  Overall, glycerol is a versatile excipient widely used in pharmaceutical formulations due to its solubilizing, moisturizing, lubricating, and stabilizing properties. Its safety profile and regulatory approval make it a preferred choice for various pharmaceutical applications.

5.6 METHANOL:

Methanol, also known as methyl alcohol or wood alcohol, is a colorless, volatile, and flammable liquid with the chemical formula CH3OH.

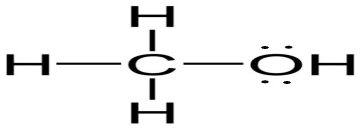


Fig.5.6 Methanol

Here's a brief drug profile of methanol:

Classification:

- Methanol is classified as a toxic alcohol due to its potential to cause severe toxicity when ingested.

Uses:

- Methanol has several industrial applications, including as a solvent, antifreeze, fuel, and in the production of formaldehyde and other chemicals.
- It is also used in laboratories as a solvent or reagent.

Toxicity:

- Methanol toxicity occurs primarily through ingestion, inhalation, or absorption through the skin.

- Upon ingestion, methanol is metabolized in the liver by alcohol dehydrogenase into formaldehyde, which is further metabolized into formic acid. Both formaldehyde and formic acid are highly toxic to the body.
- Methanol poisoning can lead to severe metabolic acidosis, visual disturbances, blindness, neurological damage, respiratory depression, and even death if not promptly treated.

Symptoms of Methanol Poisoning:

- Early symptoms may include headache, dizziness, nausea, vomiting, abdominal pain, and weakness.
- As methanol is metabolized, more severe symptoms may develop, such as visual disturbances (including blurred vision or blindness), confusion, agitation, seizures, and coma.

Treatment:

- Treatment for methanol poisoning involves several steps, including:
- Administration of ethanol or fomepizole to inhibit the metabolism of methanol to its toxic metabolites.
- Supportive care, such as intravenous fluids to correct dehydration and electrolyte imbalances.
- Hemodialysis to remove methanol and its toxic metabolites from the bloodstream**.**
- Early recognition and prompt treatment are crucial for a successful outcome in methanol poisoning cases.

Prevention:

- Preventing methanol poisoning involves education on the dangers of ingesting or inhaling methanol-containing products.
- Proper labeling and storage of methanol-containing products to prevent accidental ingestion.
- Occupational safety measures for workers handling methanol in industrial settings.

Overall, methanol is a highly toxic substance that can cause severe poisoning and even death if ingested or absorbed into the body. Awareness of its dangers, proper handling, and prompt medical treatment in cases of exposure are essential for prevention and management.

5.7 DISTILLED WATER:

Distilled water is commonly used as a solvent in various formulations across industries due to its high purity and lack of impurities. Here are some key areas where distilled water serves as a solvent:

Fig.5.7 DISTILLED WATER

Application in:

1. Pharmaceuticals
2. Cosmetics and Personal Care Products
3. Cleaning Products

4. Laboratory Reagents
5. Industrial Processes
6. Food and Beverage Industry

CHAPTER-6

MATERIALS AND METHODOLOGY

6. MATERIALS & METHODOLOGY

BOSWELLIA SERRATA: Boswellia serrata was obtained as a gift sample from Bacfo Pharmaceutical Pvt Ltd., India. All the reagents were of analytical grade. Double distilled water was used in the entire experiment.

6.1 PRE-FORMULATION PARAMETERS OF BOSWELLIA SERRATA:

6.1.1 Description: Take about 1 g of the test sample into a Petri dish and observe visually with the black background**.**It was found off-white to pale brown powder with a characteristicodor.

6.1.2 Solubility: By solubility studies,Weigh 1 part of the test sample (should not be more than 1.0 g) for each and dissolve individually in water,in alcohol,it was found that Boswellia serrata is freely soluble in methanol and insoluble in water.

6.1.3 Loss on drying:

Tare a LOD bottle with a stopper (previously dried at 105 o C for 30 minutes). Let its weight be W 1.Place about 1 g of the test sample in the dried LOD bottle, replace the stopper, and accurately weigh the bottle with its contents. Let its weight be W 2.Uniformly distribute the contents in the bottle by gentle sidewise shaking.

Place the loaded bottle in the oven, removing the stopper and leaving it also in the chamber.

Dry the contents of the LOD bottle in the oven at 105 o C ± 2°C for 2 hours.

Remove the bottle with the stopper still in its place, and allow it to cool in a desiccator before weighing.

Note: In a desiccator, care must be taken to keep the desiccant (Silica gel) fully effective by frequent replacement.

Then, record the weight of the bottle with its contents. Let its weight be W 3.

Calculation: Calculate loss on drying of the test sample in percent by the given below formula:

Loss on drying (in %) = W2-W3/W2-W1*100

Where,

W 1 = Weight of the LOD bottle (in g).

W 2 = Weight of the LOD bottle + Test sample (in g).

W 3 = Weight of the LODbottle + Test sample after drying (in g).

Limit: Not more than 5.0 % w/w.

6.1.4Assay (By Titration):

A) Total Acids

Procedure

1- Weigh accurately about 0.2g of the sample and dissolve in 30 ml Methanol by keeping on a sonicator for 5-10 minutes.

2- Titrate against 0.01N Sodium hydroxide using Phenolphthalein as indicator.

3- Perform a blank titration using methanol.

Calculation of Total Acids

Test-Blank x 0.00456× Normality of 0.01N NaOH ×100×100

Weight of sample in g x 0.01x (100-LOD)

B)-Mineral Acids

Procedure

1- Weigh accurately about 0.2g of the sample and add 100 ml of water bath. Heat the sample at70°C for 15 minutes in a water bath.

2 - Filter and collect the filtrate. Record the pH of the filtrate.

3- Take care to wash the residue on the funnel.

4- Collect the washings and filtrate in the conical flask and titrate against 0.01N Sodium hydroxideusing phenolphthalein as an indicator.

5- Perform a blank titration using methanol.

Calculation of Mineral Acids

Test Blank x 0.00365× Normality of 0.01N NaOH ×100×100

Weight of sample in g x 0.01x (100-LOD)

Boswellic Acid= Totals Acid (A) Mineral Acids (B)

Precautions:

Weigh the quantity accurately.

Wash the residue carefully to avoid any loss during titration.

6.1.5 pH (1%w/v suspension in water): The pH of the suspension of Boswellia serrata was determined by using a digital pH meter. 1gm Boswellia serrata extract dissolved in 100 ml water and pH was determined by dipping the glass electrode completely into the suspension solution system to also cover the electrode. The instrument reading pH was recorded.
Limit: 4.00 to 6.00

- **ALOE VERA:** Aloe vera was obtained as a gift sample from Bacfo Pharmaceutical Pvt Ltd., India. All the reagents were of analytical grade. Double distilled water was used in the entire experiment.

6.2 PRE FORMULATION PARAMETERS OF ALOE VERA:

6.2.1 Description: Take about 1 g of the test sample into a Petri dish and observe visually with a black back ground**.** It was found brown colored powder with a bitter taste.

6.2.2 Solubility: By solubility studies,Weigh 1 part of the test sample (should not be more than 1.0 g) for each and dissolve individually in water, in alcohol, it was found that aloe vera is freely soluble in water and insoluble in alcohol.

6.2.3 Loss on drying:

Tare a LOD bottle with a stopper (previously dried at 105 o C for 30 minutes). Let its weight be W 1.Place about 10 g of the test sample in the dried LOD bottle, replace the stopper, and accurately weigh the bottle with its contents. Let its weight be W2.Uniformly distribute the contents in the bottle by gentle sidewise shaking.

Place the loaded bottle in the oven, removing the stopper and leaving it also in the chamber.

Dry the contents of the LOD bottle in the oven at 105 o C ± 2°C for 1 hour.

Remove the bottle with the stopper still in its place, and allow it to cool in a desiccator before weighing.

Note: In a desiccator, care must be taken to keep the desiccant (Silica gel) fully effective by frequent replacement.

Then, record the weight of the bottle with its contents. Let its weight be W 3.

Calculation: Calculate loss on drying of the test sample in percent by the given below formula:

Loss on drying (in %) = W2-W3/W2-W1*100

Where,

W 1 = Weight of the LOD bottle (in g).

W 2 = Weight of the LOD bottle + Test sample (in g).

W 3 = Weight of the LOD bottle + Test sample after drying (in g).

Limit: Not more than 8.0 % w/w.

6.2.4 pH (1%w/v in water): The pH of the suspension of Boswellia serrata was determined by using a digital pH meter. 1gm aloe vera extract dissolved in 100 mlv water and pH was determined by dipping the glass electrode completely into the suspension solution system to also cover the electrode. The instrument reading pH was recorded.

Limit: 4.00 to 7.00

6.2.5 Forming Index: One gm of coarse powder was weighted and transferred to a 500 ml conical flask containing 100 ml of water. It was maintained at moderate boiling for 30 minutesina water bath. It was cooled and filtered into a 100 ml volumetric flask. Volume was diluted by adding a sufficient amount of water. The decoction was poured intothe test

tube and then shaken in a lengthwise motion for 15 seconds. They were allowed to stand for 15 minutes and the height of foam was measured to determine the foaming index.

6.3 FORMULATION OF MICROSPHERE:

STEP 1: Firstwe take a 45ml of methanol and 5 ml of water in a beaker on a magnetic stirrer with a bead.

STEP 2: The weighed quantity of drug will be dissolved pinch by pinch in a beaker and the rotation isadjusted to 500rpm.

STEP 3: After the drug, we will add HPMC polymer in a small quantity and increase the speed up to 600rpm.

STEP 4: The weighed quantity of Ethyl Cellulose is added to the beaker. So, here we getting a homogenized mixture of the two polymers and drug.

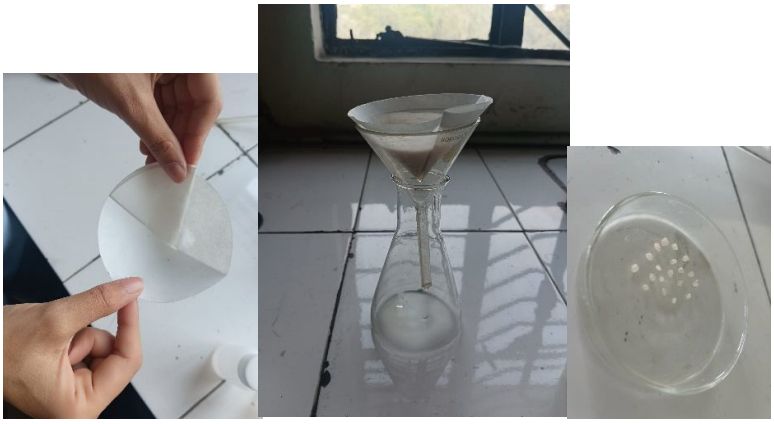
HPMC and Ethyl cellulose will start embedding the drug in its core.

STEP 5: We have a propeller installed and have taken around 100ml of glycerol in a beaker set the rotation and stirred it.

When the glycerol is stirred at a particular speed and methanol has dissolved in the drug and polymer and after that stop the mechanical stirrer and remove the bead.

STEP 6: A syringe is used,where the quantity of methanol along with the polymer is filled into the syringe. So it is done by Injection method.
In this method, drop by drop of polymer and drug mixture is added into the glycerol and the solvent will evaporate.

STEP 7: After the particular time of period about half an hour, we get discrete spherical microspheres which are settled down into the base, then we just filter by using Whatman filter paper and dry in a hot air oven.



6.4 EVALUATION PARAMETERS OF MICROSPHERE:

1. % yield of microspheres: Thoroughly dried microspheres were collected and weighed accurately. The percentage yield was then calculated using the formula given below,

a. % Yield = mass of microsphere obtained / total weight of drug & polymer X 100.

2. Bulk density: This is determined by pouring perceived microspheres into a graduated cylinder via a large funnel and measuring the volume and weight.

3. Tapped density A known weight of the microspheres was transferred to a measuring cylinder, tapped manually 100 times, and the ratio of weight to volume of the microspheres gives the tapped density.

4.Carr's index: It was measured by using the following formula,

a. Carr's Index = {(Vb –Vt) / Vb}* 100 b.

Where, c. Vb and Vt are the bulk volume and tapped volume respectively.

5. Encapsulation Efficiency (%) = [(Amount of B. serrata extract in microspheres) / Total amount added] x 100.

6. Drug loading (%) = (Amount of B. serrata extract in microspheres) / Weight of microspheres] x 100.

7.Particle size distribution of microsphere: The size of the prepared microspheres was measured by the optical microscopy method using a calibrated stage micrometer. It is carried out by using a compound microscope at 10 axis lower and 6axis upper lances. Dried microspheres were first re-dispersed in distilled water and placed in a glass slide and the number of divisions of calibrated eyepiece was counted by a micrometer using a stage micrometer. The average size of 100 particles was determined by the given equation.

Mean particle size=Total sum of particle size/Total number of particle size

8.Swelling studies: A known weight (50 mg) of microspheres were placed in a glass vial containing 10 ml of distilled water at 37 ± 0.50C in an incubator with occasional shaking. The microspheres were periodically removed, blotted with filter paper and their changes in weights were measured during the swelling until equilibrium was attained. Finally, the weight of the swollen microspheres was recorded after a period of 3 hours, and the swelling ratio (SR) was then calculated from the following formula.

SR=We-Wo / Wo

Where, Wo = Initial weight of the dry microspheres,

We = Weight of the swollen microspheres at equilibrium swelling in the media.

9. In Vitro drug studies: Dissolution studies were carried out for the microspheres, employing USP XXIII apparatus (Basket method) at 37± 0.5 0C rotated at 100 rpm using suitable dissolution medium. A sample of microspheres was used in each test. An aliquot of the sample was periodically withdrawn at suitable time interval and the volumes were replaced with fresh dissolution medium in order to maintain the sink condition. The sample was analyzed spectrophotometrically at suitable 274 nm.

$$\frac{\text{Test absorbance}}{\text{Standard absorbance}} \times \frac{\text{Concentration of Standard}}{\text{Concentration of Test}} \times 100$$

CHAPTER- 7

RESULTS AND DISCUSSION

7. RESULT & DISCUSSION

TABLE 7.1- PREFORMULATION STUDIES OF BOSWELLIA SERRATA.

Sr.No	Parameter	Results
1.	Description	off-white to pale brown powder
2.	Solubility	freely soluble in methanol and insoluble in water
3.	LOD	3.58
4.	Assay (By Titration)	71.5
5.	pH	4.72

TABLE 7.2- PREFORMULATION STUDIES OF ALOE VERA.

Sr.No	Parameter	Results
1.	Description	Brown-colored powder with a bitter taste.
2.	Solubility	freely soluble in water and insoluble in alcohol
3.	LOD	5.21
4.	pH	4.62
5.	Foaming Index	0.59

TABLE 7.3- FORMULATION OF MICROSPHERES.

Formulation	HPMC:EC	Boswellia serrata(mg)	Aloe vera (mg)	Solvent
F1	25:2.5	25	25	H_2O :MeOH
F2	30:5	30	30	H_2O :MeOH
F3	35:10	35	35	H_2O :MeOH
F4	40:15	40	40	H_2O :MeOH
F5	45:20	45	45	H_2O :MeOH

TABLE 7.4-Percentage Yield obtained for each formulation of Boswellia serrata and Aloe vera extract loaded microspheres.

Formulation	Weight of Microspheres	Weight of Excipients+Weight of Drug (mg)	Percentage of yield (%)
F1	25.4	77.5	32.77
F2	38.7	95	40.73
F3	48.6	115	42.26
F4	52.5	135	38.89
F5	55.4	155	35.74

Graphical Representation:

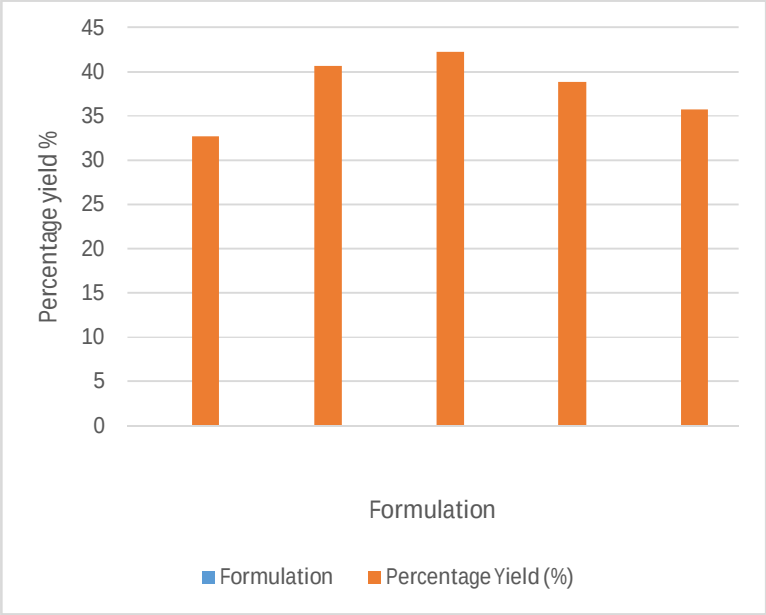


TABLE 7.5-Percentage of Entrapment efficiency of Boswellia serrata and Aloe vera extract-loaded microspheres.

Formulation	Weight of Boswellia serrata and Aloe vera extract (mg)	Weight of Boswellia serrata and Aloe vera extract in microsphere (mg)	Percentage of Entrapment efficiency (%)
F1	77.5	39.2	50.58
F2	95	47.9	50.42
F3	115	60.0	52.17
F4	135	72.4	53.62
F5	155	90.2	58.19

Graphical Representation:

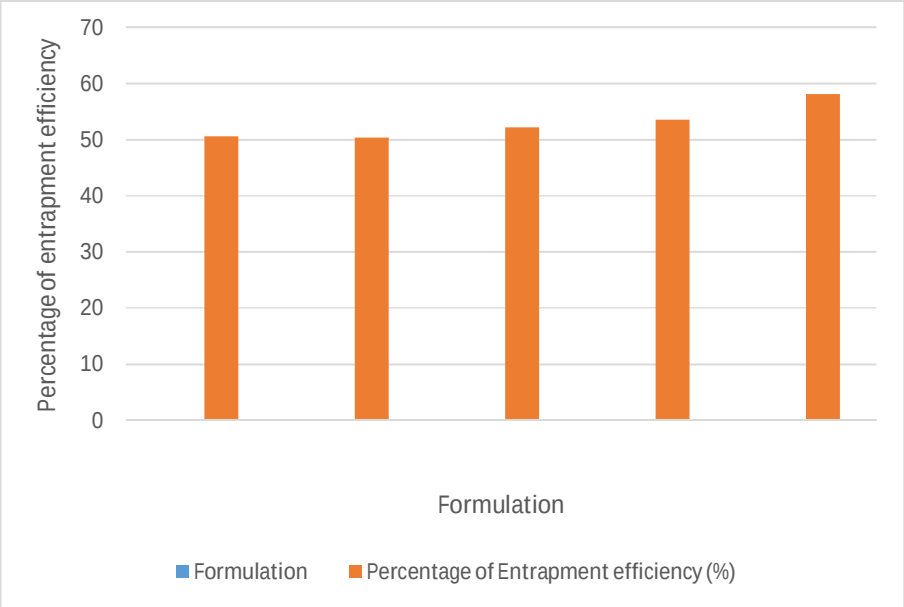


TABLE 7.6-Drug loading of Boswellia serrata and Aloe vera extract-loaded microspheres.

Formulation	Drug loading
F1	154.3
F2	123.7
F3	123.4
F4	137.9
F5	162.8

Graphical Representation:

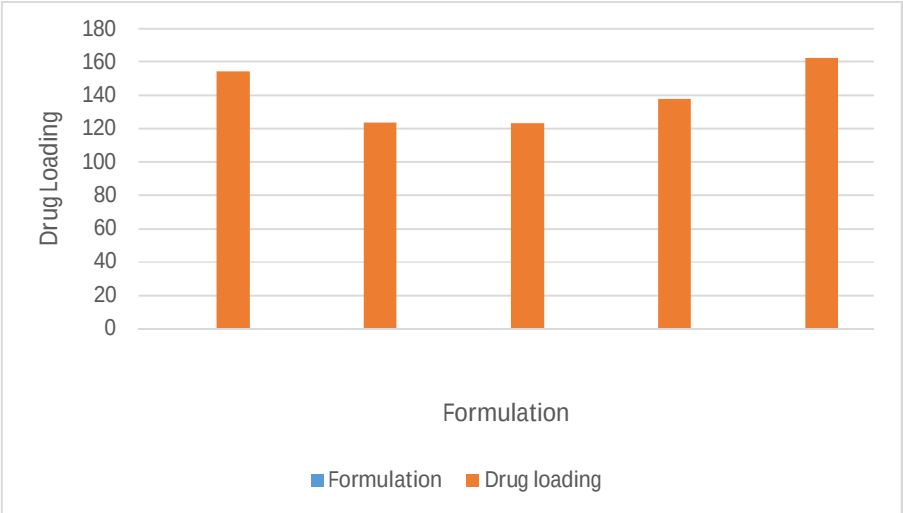


TABLE 7.7-Particle size of Boswellia serrata and Aloe vera extract-loaded microspheres.

Formulation	Particle Size
F1	54.62
F2	63.82
F3	68.92
F4	49.98
F5	53.4

Graphical Representation:

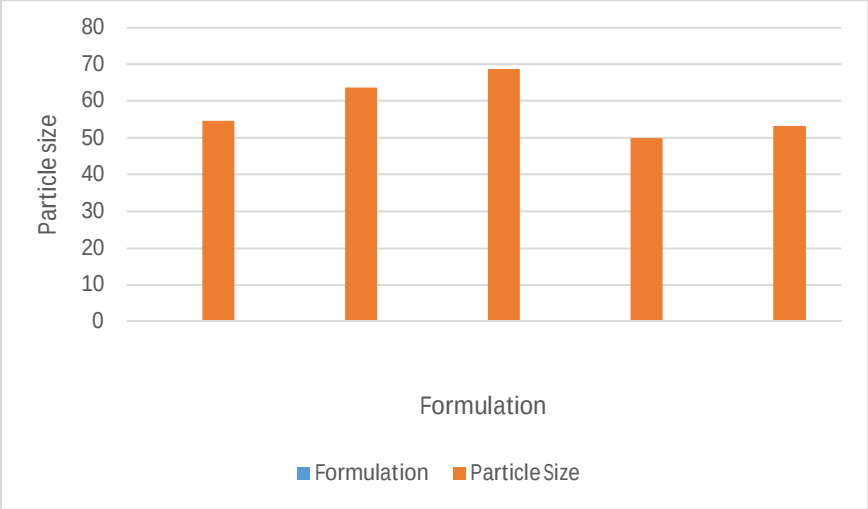


TABLE 7.8-Swelling Index of Boswellia serrata and Aloe vera extract loaded microspheres.

Formulation	Initial weight of Microsphere	Final weight of Microsphere	Swelling Index
F1	25.4	28.9	0.13
F2	38.7	41.9	0.08
F3	48.6	52.4	0.07
F4	52.5	55.6	0.05
F5	55.6	58.3	0.04

Graphical Representation:

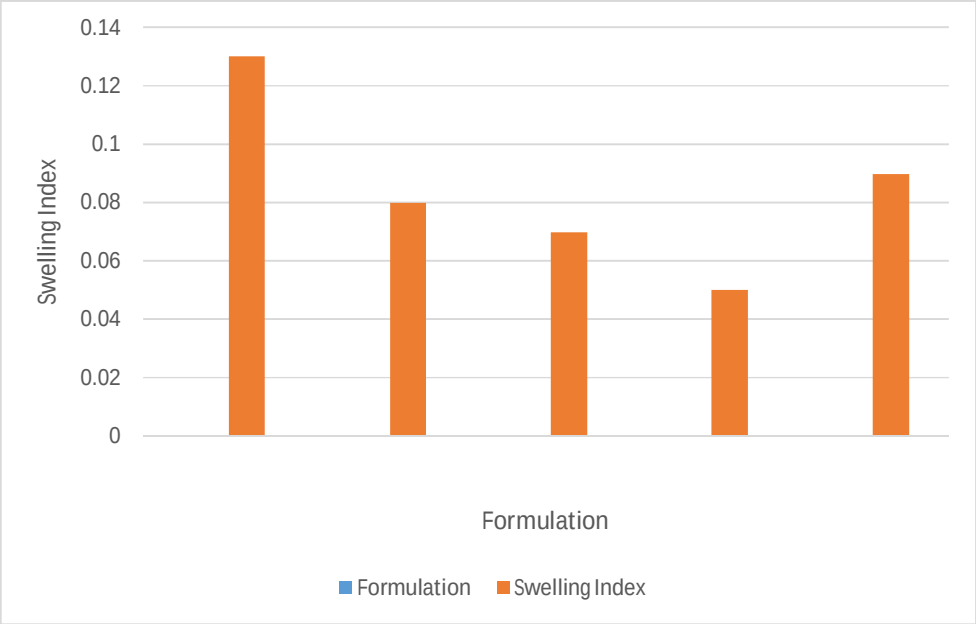


TABLE 7.9 -In Vitro drug release of Boswellia serrata and Aloe vera extract loaded microspheres.

Time (min)	F1		F2		F3		F4		F5	
	Abs	Drug release (%)	Abs	Drug release (%)	Abs	Drug release (%)	Abs	Drug release (%)	Abs	Drug release (%)
30 min	0.251	44.724	0.266	47.396	0.278	49.794	0.289	51.764	0.450	80.602
60 min	0.260	46.327	0.275	49.0	0.266	48.944	0.292	53.728	0.459	84.456
90 min	0.267	47.575	0.286	50.96	0.267	49.128	0.301	54.18	0.468	86.112
120 min	0.272	48.465	0.291	51.851	0.275	50.6	0.298	54.832	0.476	87.584
150 min	0.281	50.069	0.297	52.92	0.284	52.256	0.294	54.096	0.492	90.528

TABLE 7.10 -In Vitro drug release of formulation 1.

Calculation:

AT 30 MIN		0.251	49	5	100	100
		0.55	100	50	5	
RESULT	**44.724**					
AT 60MIN		0.260	49	5	100	100
		0.55	100	50	5	
RESULT	**46.327**					
AT 90 MIN		0.267	49	5	100	100
		0.55	100	50	5	
RESULT	**47.575**					
AT 120MIN		0.272	49	5	100	100
		0.55	100	50	5	
RESULT	**48.465**					
AT 150MIN		0.281	49	5	100	100
		0.55	100	50	5	
RESULT	**50.069**					

TABLE 7.11 -In Vitro drug release of formulation 2.

AT 30 MIN		0.266	49	5	100	100
		0.55	100	50	5	
RESULT	**47.396**					
AT 60MIN		0.275	49	5	100	100
		0.55	100	50	5	
RESULT	**49**					
AT 90 MIN		0.286	49	5	100	100
		0.55	100	50	5	
RESULT	**50.96**					
AT 120MIN		0.291	49	5	100	100
		0.55	100	50	5	
RESULT	**51.851**					
AT 150MIN		0.297	49	5	100	100
		0.55	100	50	5	
RESULT	**52.92**					

TABLE 7.12 -In Vitro drug release of formulation 3.

AT 30 MIN		0.278	50.6	5	100	100
		0.565	100	50	5	
RESULT	**49.794**					

AT 60MIN		0.266	50.6	5	100	100
		0.565	100	50	5	
RESULT	**47.645**					
AT 90 MIN		0.267	50.6	5	100	100
		0.565	100	50	5	
RESULT	**47.824**					
AT 120MIN		0.275	50.6	5	100	100
		0.565	100	50	5	
RESULT	**49.257**					
AT 150MIN		0.284	50.6	5	100	100
		0.565	100	50	5	
RESULT	**50.869**					

TABLE 7.13 -In Vitro drug release of formulation 4.

AT 30 MIN		0.289	50.6	5	100	100
		0.565	100	50	5	
RESULT	**51.764**					
AT 60MIN		0.292	50.6	5	100	100
		0.55	100	50	5	
RESULT	**52.302**					
AT 90 MIN		0.301	49.5	5	100	100
		0.55	100	50	5	
RESULT	**52.742**					
AT 120MIN		0.298	50.6	5	100	100
		0.55	100	50	5	
RESULT	**53.376**					
AT 150MIN		0.294	50.6	5	100	100
	52.66	0.565	100	50	5	
RESULT						

TABLE 7.14 -In Vitro drug release of formulation 5.

AT 30 MIN		0.45	50.6	5	100	100
		0.565	100	50	5	
RESULT	**80.602**					
AT 60MIN		0.459	50.6	5	100	100
		0.565	100	50	5	
RESULT	**82.214**					
AT 90 MIN		0.468	50.6	5	100	100
		0.565	100	50	5	
RESULT	**83.826**					

AT 120MIN		0.476	50.6	5	100	100
		0.565	100	50	5	
RESULT	**85.259**					
AT 150MIN		0.492	50.6	5	100	100
		0.565	100	50	5	
RESULT	**88.125**					

CHAPTER- 8

CONCLUSIONS

8. CONCLUSION

In conclusion, Formulating and evaluating Boswellia serrata and Aloe vera microparticles for the treatment of ulcerative colitis represents a significant advancement in therapeutic strategies aimed at managing this chronic inflammatory condition of the gastrointestinal tract. Ulcerative colitis (UC) is characterized by inflammation and ulceration of the mucosal lining of the colon and rectum, leading to symptoms such as abdominal pain, diarrhea, and rectal bleeding. Current treatments often involve medications that suppress the immune response or reduce inflammation systemically, which can have significant side effects and may not be effective for all patients. Therefore, there is a growing interest in developing targeted and more efficacious therapies for UC, such as Boswellia serrata and Aloe vera microparticles.

Boswellia serrata, commonly known as Indian frankincense, has been traditionally used in Ayurvedic medicine for its anti-inflammatory properties. It contains boswellic acids, which inhibit pro-inflammatory enzymes and cytokines, thereby reducing inflammation in the gastrointestinal tract. Aloe vera, a succulent plant with mucilage-rich leaves, is renowned for its wound-healing and anti-inflammatory effects. It contains polysaccharides, glycoproteins, and other bioactive compounds that promote tissue repair and modulate immune responses locally.

The formulation of Boswellia serrata and Aloe vera into microparticles offers several advantages over conventional dosage forms. Microparticles are typically designed to encapsulate the active ingredients, protecting them from degradation in the acidic environment of the stomach and ensuring controlled release in the colon, where inflammation occurs in UC. This targeted delivery system enhances bioavailability and reduces the frequency of dosing, thereby improving patient compliance and therapeutic outcomes.

The evaluation of these microparticles involves several critical parameters to assess their suitability and efficacy. Physicochemical characterization includes determining particle size, morphology, drug loading efficiency, and in vitro release profiles under simulated physiological conditions. Pharmacokinetic studies help understand the absorption, distribution, metabolism, and excretion of the active compounds, while pharmacodynamic evaluations assess their therapeutic effects in animal models of UC.

Studies have shown that Boswellia serrata and Aloe vera microparticles exhibit promising therapeutic potential in preclinical models of UC. They have been observed to reduce inflammation, promote mucosal healing, and improve clinical symptoms such as diarrhea and rectal bleeding. Furthermore, their localized action in the colon minimizes systemic exposure and reduces the risk of systemic side effects commonly associated with conventional therapies.

The safety profile of these microparticles is also a crucial consideration. While Boswellia serrata and Aloe vera are generally regarded as safe, ensuring the absence of toxic effects and potential allergens in the microparticle formulation through rigorous toxicity studies is essential prior to clinical trials. Moreover, assessing long-term efficacy and stability

under various storage conditions will determine the feasibility of scaling up production for clinical use.

The formulation and evaluation of Boswellia serrata and Aloe vera microparticles represent a promising approach for the treatment of ulcerative colitis. Their targeted delivery, enhanced bioavailability, and favorable safety profile make them potential candidates for future therapeutic strategies aimed at improving the management of this challenging inflammatory bowel disease. Further clinical studies are warranted to validate their efficacy and safety in human subjects, paving the way for their eventual integration into mainstream clinical practice as a novel treatment option for UC patients.

CHAPTER- 9

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9.REFERENCES

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PUBLICATIONS

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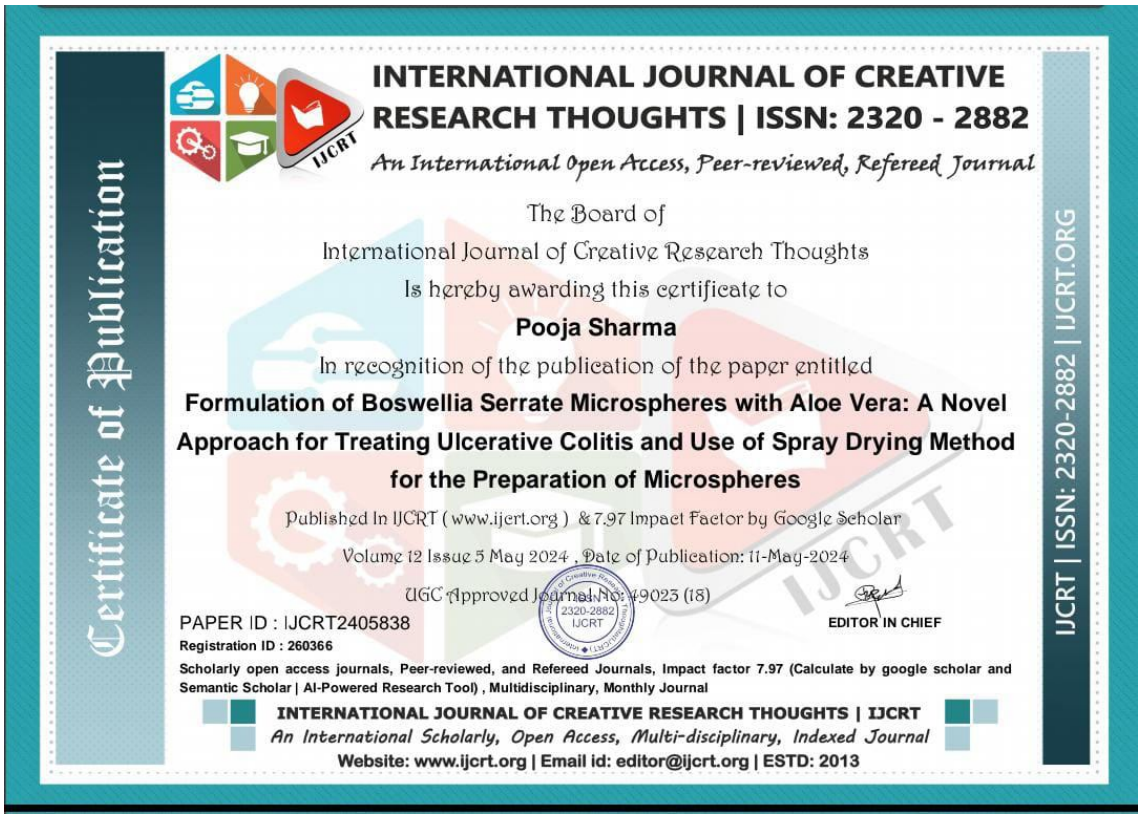
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RESUME

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CAREER OBJECTIVE

Work for an organisation which provides me the opportunity to improve my knowledge and skills to growth along with the organisation.

BRIEF OVERVIEW

STRENGTHS

Effective Communication skill

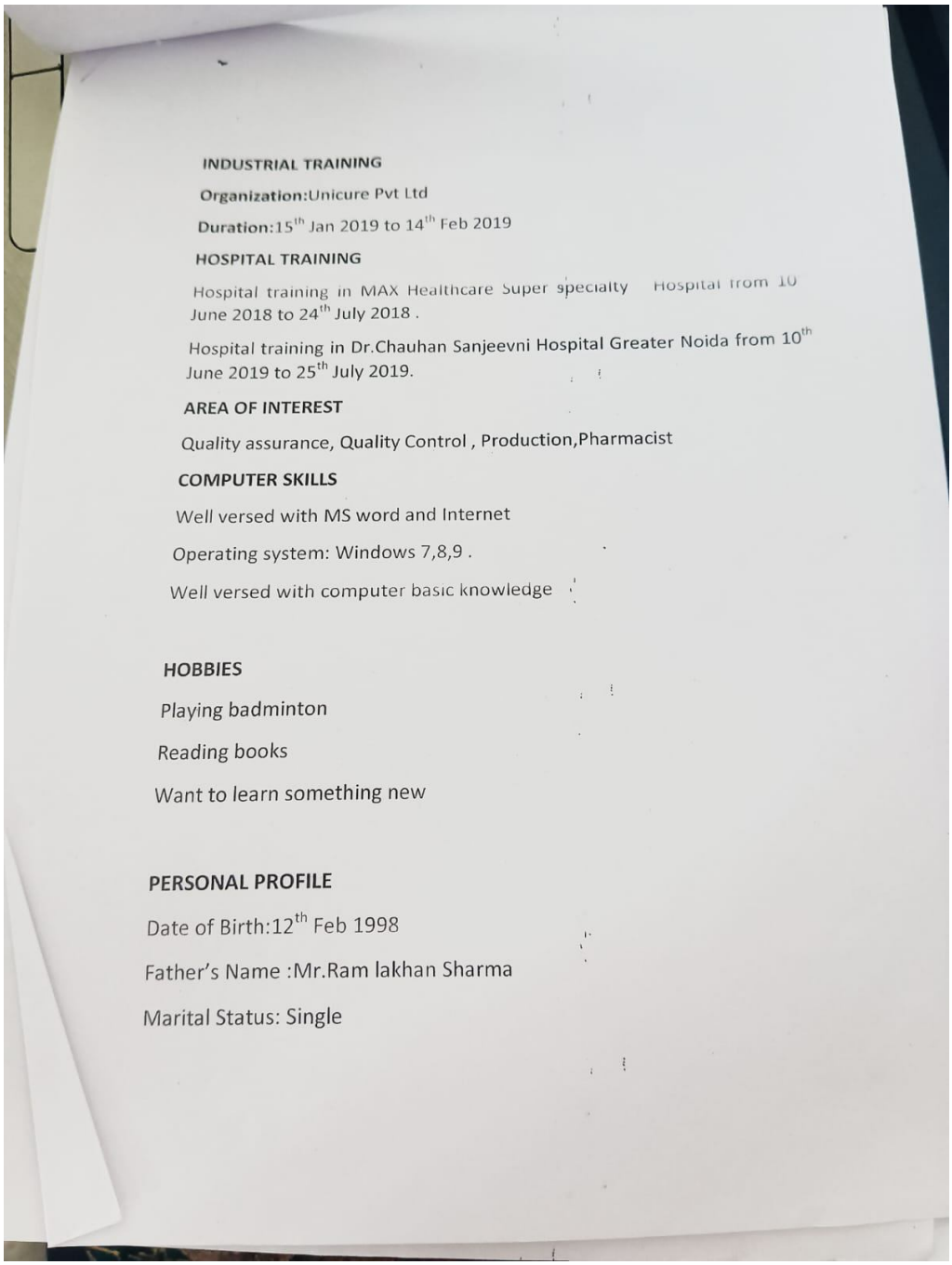
Hardworking

Positive learner

Quick learner

ACADEMIC CREDENTIALS

Year	Education	Division	Board/University
2014	High school	1st	CBSE
2016	Intermediate	1st	CBSE
2016-2020	B.pharma	1 division with hons	Rameesh institute of vocational and technical education (Aktu)



INDUSTRIAL TRAINING

Organization: Unicure Pvt Ltd

Duration:15th Jan 2019 to 14th Feb 2019

HOSPITAL TRAINING

Hospital training in MAX Healthcare Super specialty Hospital from 10 June 2018 to 24th July 2018 .

Hospital training in Dr.Chauhan Sanjeevni Hospital Greater Noida from 10th June 2019 to 25th July 2019.

AREA OF INTEREST

Quality assurance, Quality Control , Production,Pharmacist

COMPUTER SKILLS

Well versed with MS word and Internet

Operating system: Windows 7,8,9 .

Well versed with computer basic knowledge

HOBBIES

Playing badminton

Reading books

Want to learn something new

PERSONAL PROFILE

Date of Birth:12th Feb 1998

Father's Name :Mr.Ram lakhan Sharma

Marital Status: Single

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Certified that **Pooja Sharma** (Enrollment no.**220227056061771**) has carried out the research work presented in this thesis entitled "**Formulation And Evaluation of Boswellia Serrata And Aloe Vera Microsphere For Ulcerative Colitis Treatment** " for the award of **MasterofPharmacy** from Dr. APJ Abdul Kalam Technical University, Lucknow under my/our supervision. The thesis embodies results of original work, and studies are carried out by the student herselfand the contents of the thesis do not form the basis for the award of any other degree to the candidate or to anybody else from this or any other University/Institution

21/07/24

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Professor

Innovative College of Pharmacy

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