WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.453
Volume 15, Issue 2, 270-289. Review Article ISSN 2277–7105

HERBAL BIOACTIVES IN GUT-TARGETED DRUG DELIVERY: A REVIEW OF *PANAX QUINQUEFOLIUS*–LOADED HYDROGEL MICROSPHERE

***Pradeep Kumar, Dr. Abhishek Kumar, Ashu Goel, Kajal Rani**

Department of Pharmacy, ABSS Institute of Technology, Salarpur NH-119 (Delhi NCR) Meerut, Uttar Pradesh, India, 250001.

Article Received on 15 Dec. 2025,
Article Revised on 05 Jan. 2026,
Article Published on 16 Jan. 2026,

https://doi.org/10.5281/zenodo.18256602

***Corresponding Author**

Pradeep Kumar

Department of Pharmacy, ABSS Institute of Technology, Salarpur NH-119 (Delhi NCR) Meerut, Uttar Pradesh, India, 250001.

How to cite this Article: *Pradeep Kumar, Dr. Abhishek Kumar, Ashu Goel, Kajal Rani (2026). Herbal Bioactives In Gut-Targeted Drug Delivery: A Review Of Panax Quinquefolius–Loaded Hydrogel Microsphere. World Journal of Pharmaceutical Research, 15(2), 270–289.

ABSTRACT

These days, the gut microbiota is crucial to human health, affecting metabolism, immunity, and neurobehavioral control, among other physiological systems. Recent developments in gut-targeted drug delivery methods have made it possible to precisely alter microbial composition to treat and prevent gastrointestinal and systemic diseases. Panax L. Quinquefolius. The pharmacologically active ginsenosides found in the popular medical herb "American ginseng" have significant anti-inflammatory, antioxidant, immunomodulatory, and microbiota-regulating qualities. However, ginsenosides' bioavailability and localized release pose problems because of their vulnerability to breakdown and inadequate absorption in the upper gastrointestinal tract. This study explores the development of hydrogel microspheres as a viable delivery method to enhance the stability of P. quinquefolius extracts and permit controlled release at the intended gut region. Among the formulation methods that are thoroughly investigated are inotropic gelation, emulsion crosslinking, and spray drying. Preformulation studies are essential for improving drug release kinetics, swelling behaviour, encapsulation efficiency, and particle size. This study examines how hydrogel microspheres can directly impact gut microbial populations and restore microbial balance in relation to gastrointestinal illnesses, metabolic syndrome, and issues related to the gut-brain axis. Combining plant-derived bioactives with cutting-edge polymer-based delivery methods offers a synergistic approach to

creating medical medicines that target the microbiota. This research highlights the therapeutic potential of P. quinquefolius-loaded hydrogel microspheres and offers a thorough analysis of their composition, assessment, and potential uses in microbiome-targeted drug delivery.

KEYWORDS: P. Quinquefolius, Gut health, Ginsenosides, Microsphere.

Review Methodology

Herbal bioactives, hydrogel microsphere-based targeted drug delivery systems, and gut microbiota manipulation were the main topics of this review article's thorough and methodical literature assessment. In order to gather pertinent research articles, reviews, and original research papers, scientific databases like PubMed, Science Direct, Google Scholar, and Scopus were thoroughly searched.

Panax quinquefolius L., ginsenosides, gut microbiota, hydrogel microspheres, colon-targeted drug delivery, and herbal bioactives were among the terms used both separately and in combination. We took into consideration peer-reviewed studies that were published primarily between 2010 and 2024. Excluded were studies that concentrated on non-oral methods, non-herbal drug delivery systems, or unrelated microbiome interventions. An updated and thorough overview of microbiome-targeted hydrogel microsphere systems was produced by critically analysing and summarizing the chosen literature.[1,2]

1. INTRODUCTION

The oral medication delivery system is the recommended method due to its ease of administration, non-invasiveness, high patient compliance, and variety in formulation. Conventional oral dose formulations provide a particular pharmaceutical concentration into the systemic circulation without regulating drug distribution. Since these methods only produce and sustain drug concentrations within the therapeutically effective range required for therapy when administered multiple times daily, they lead to notable fluctuations in drug levels in the systemic circulation. Oral medicine is often used as needed for the long-term management of numerous chronic conditions.[3]

1.2 Targeted Drug Delivery Systems

The objective of any drug delivery system is to ensure that the proper drug concentration is rapidly attained and then sustained while delivering a therapeutic dose of medication to the appropriate site in the body. The drug delivery system must administer medication at a pace

set by the body's requirements over a predefined period of time. Site-specific medication delivery is the direct targeting of a pharmacological compound to a specific biological location. Targeted drug delivery is the accurate and efficient localization of a drug at therapeutic concentrations within the desired target while reducing exposure to non-target regions. A tailored drug delivery approach is advantageous in the following scenario.[4]

1.3 Gut Microbiome

The term "gut microbiome" refers to the intricate group of trillions of bacteria, viruses, fungi, and archaea that reside in the human gastrointestinal tract, primarily in the colon. These microorganisms are both passive inhabitants and active contributors to several physiological functions, including immunological control, digestion, nutrition metabolism, and the synthesis of neurochemicals. Over the past ten years, the gut microbiota has become a prominent therapeutic target for several gastrointestinal and systemic disorders. The term "microbiota" was originally used in the early 1900s. The stomach, skin, lungs, oral cavity, and other areas of the human body are home to a variety of microorganisms, such as bacteria, yeasts, and viruses. Often referred to as "the hidden organ," the human microbiota provides over 150 times the genetic information of the entire human genome.[5]

Despite the fact that the terms "microbiota" and "microbiome" are sometimes used interchangeably, they differ significantly. The phrase "microbiota" refers to the living microorganisms present in a certain habitat, such as the oral and gastrointestinal microbiota. The term "microbiome" refers to the collection of genomes from all microbes in an ecosystem, including the microbial population, structural components, metabolites, and environmental factors.[6] The microbiome composition varies depending on the location. The gut microbiota is considered to be the most crucial component in preserving human health.[7]

The gut microbiota performs a variety of tasks, including food fermentation, pathogen defense, immune response activation, and vitamin synthesis.

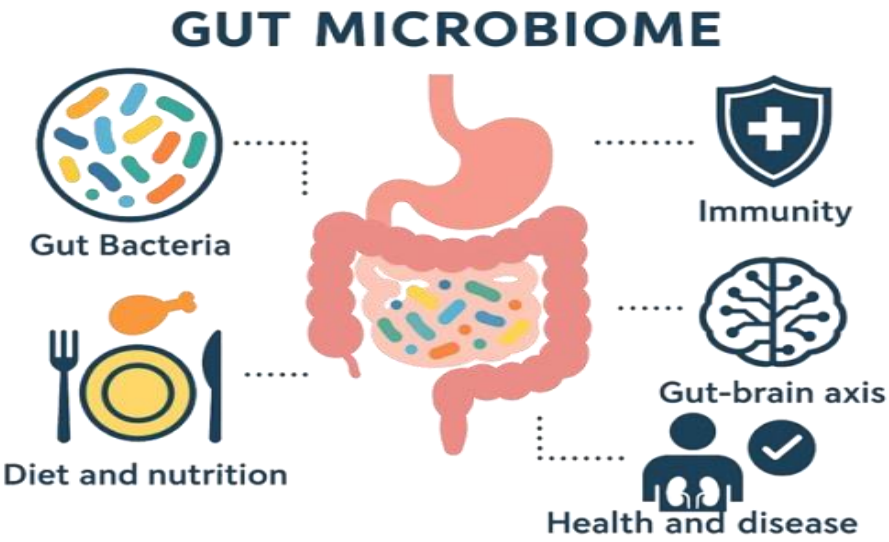

Figure 1: Diagram illustrating the human gut microbiome and its major functions. Gut bacteria influence digestion, immune response, the gut-brain axis, and overall health. Diet and nutrition play a crucial role in maintaining microbial balance.

1.4 Composition and Role of the Gut Microbiome

Dominant bacterial phyla: Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria.

Functions

The gut microbiota carries out a number of critical tasks that are necessary for preserving health. Short-chain fatty acids (SCFAs), which are essential for gut health and energy metabolism, are produced by fermenting indigestible food fibers. It also helps to preserve the integrity of the mucosa by regulating the intestinal barrier. Furthermore, the microbiota is crucial for the growth and regulation of the immune system and affects both innate and adaptive responses. It aids in the production of vital vitamins like vitamin B12 and vitamin K and is involved in the metabolism of bile acids as well as the detoxification of xenobiotics. Furthermore, through neurotransmitter regulation, the gut microbiota affects the gut–brain axis, which affects mood, cognition, and general neurological function.

1.5 Strategies to Modify the Gut Microbiome[8, 9]

1. Dietary Interventions

Diet has a major impact on the microbiota's composition. Fiber-rich diets promote the development of beneficial bacteria that produce SCFAs, such as butyrate. Polyphenol-rich foods, like ginseng, berries, and green tea, serve as prebiotics and boost microbial diversity.

2. Prebiotics

Non-digestible dietary ingredients like inulin and fructooligosaccharides that especially promote the growth of beneficial microorganisms. Encourage the production of SCFA and improve the gut barrier's performance.

3. Probiotics Lactobacillus and Bifidobacterium are live, beneficial bacteria that help restore microbial equilibrium. Used to treat diarrhoea, IBD, and urogenital infections.

4. Synbiotics a blend of prebiotics and probiotics for complementary benefits.

5. Fecal Microbiota Transplantation (FMT)

Giving a sick individual the excrement of a healthy donor can restore microbial diversity. Proven effectiveness in treating Clostridium difficile infections that reoccur. Research is being done on neurological disorders, obesity, and IBD.

6. Antibiotics and Microbiome Reset

Broad-spectrum antibiotics may alter the microbiota's composition, but they may also have detrimental long-term impacts. Used with caution in some circumstances, such as SIBO (small intestinal bacterial overgrowth).

7. Herbal Compounds and Phytochemicals

Plant-based bioactives like ginsenosides (from Panax quinquefolius) have an effect on the gut flora. Can alter the makeup of bacteria and strengthen the intestinal barrier. Act as anti-inflammatory and immunomodulatory medications.

1.6 Role of Herbal Bioactives in Gut-Targeted Delivery

Due to their potential to improve gastrointestinal health and change the gut microbiota, herbal bioactives—phytochemicals derived from medicinal plants—have garnered a lot of attention. Many natural compounds, such as ginsenosides, curcuminoids, flavonoids, alkaloids, and polyphenols, have anti-inflammatory, antioxidant, prebiotic, and antibacterial properties. However, while the colon is the primary site of microbiota interaction, limited solubility, rapid absorption in the upper GI tract, and enzymatic degradation sometimes limit their effectiveness. To overcome these limitations, scientists are actively researching gut-targeted drug delivery techniques, such as hydrogel microspheres, to effectively and selectively convey herbal bioactives to the large intestine.

Table 1: List of some bio herbal bioactive compound and there activity

S.No	Herbal Bioactive	Source Plant	Activity	Gut-Targeted System Used
1	**Ginsenosides**	*Panax quinquefolius*	Microbiome modulation, immunity	Hydrogel microspheres, nanoparticles
2	**Curcumin**	*Curcuma longa*	Anti-inflammatory, antioxidant	Pectin-coated microspheres
3	**Berberine**	*Berberis aristata*	Antimicrobial, antidiabetic	pH-sensitive polymer capsules
4	**Quercetin**	Various fruits	Anti-inflammatory, prebiotic	Colon-targeted hydrogel beads
5	**Resveratrol**	Grapes, berries	Anti-inflammatory, antioxidant	Alginate-chitosan hydrogel beads

By controlling the gut flora, ginseng, or Panax quinquefolius, can help treat gastrointestinal and neurological conditions. It can do this by: Probiotic bacteria like Bacteroides and Lactobacillaceae are becoming more prevalent. Lowering the frequency of dangerous bacteria like Proteobacteria and Helicobacteraceae Increasing the Firmicutes to Bacteroidetes phylum ratio increasing the overall concentration of SCFA, which consists of acetic acid, butyric acid, and propionic acid The concept of a targeted drug delivery system is frequently used in anti-cancer drugs. A targeted medication delivery system usually consists of a targeted unit and a cargo unit. The targeted units offer high ligand-binding efficiency to the targeted tissue or cells, while the cargo units are the bioactive drugs that are sometimes included into vehicles like liposomes and nanoparticles.

Role of herbal bioactive in gut-Targeted delivery

Figure: 2 Mechanism of Gut-Targeted Delivery of Herbal Bioactives: Illustration showing how herbal compounds like ginsenosides from *Panax quinquefolius* interact with the gut microbiota when delivered via targeted.

Tailored medicine administration has recently been used in the realm of specific antibacterial drugs. A novel intracellular antibiotic delivery mechanism was found in a recent study. The delivery approach consists of three parts: mesoporous silica nanoparticles loaded with gentamicin, lipid bilayer envelopes that scatter upon interaction with S. aureus hemolysins, and a S. aureus-targeting domain derived from the previously reported antibacterial peptide ubiquicidin. An antibody that targets S. aureus was mixed with lipid nanoparticles containing an antibiotic in an alternate drug delivery method. The resultant system showed enhanced in vitro bactericidal efficacy against S. aureus in both planktonic and biofilm phases. To alter the microbiome, particularly to reduce pathobionts in the gut, narrow-spectrum antimicrobial drugs are utilized.[10, 11]

1.7 Advantages of Hydrogel Microspheres for Herbal Bioactives

Targeted distribution at colonic pH (about 7.4) is made possible by the formulation's pH-sensitive medication release. Its potent mucoadhesive qualities increase therapeutic efficacy by ensuring extended retention at the site of action. The technology is safe to employ in pharmaceutical applications because it is non-toxic and biocompatible. Its regulated medicine release profile also enables long-term therapeutic dosages. Additionally, the formulation protects the medicine against enzymatic and acidic breakdown, ensuring its stability throughout the gastrointestinal tract.

Table: Comparison of Gut-Targeted Drug Delivery Systems.[12, 13]

Delivery System	Advantages	Limitations
Hydrogel microspheres	pH-sensitive release, biocompatible, mucoadhesive	Scale-up complexity
Nanoparticles	High surface area, enhanced absorption	Potential toxicity
Liposomes	Good biocompatibility	Physical instability
Matrix tablets	Simple formulation	Poor site specificity
Prodrug approach	Improved targeting	Complex synthesis

1.8 Ginsenosides as Bioactives

Ginsenosides are the primary active components of Panax species, including Panax quinquefolius L. (American ginseng). The naturally occurring triterpene saponins in ginseng are responsible for the majority of its pharmacological benefits, including its anti-inflammatory, immunomodulatory, neuroprotective, antidiabetic, and gut microbiota-regulating properties.Rg1, Re, Rb1, Rc, Rd, and Rg3 are the most researched of the more

than thirty ginsenosides that have been discovered. The hydrophobic steroidal backbone and one or more sugar moieties that comprise their composition affect their solubility, stability, and bioavailability.

1.9 Pharmacological Activity

Table 2: Pharmacological Activity of Ginsenosides.

Activity	Key Effects
Immunomodulation	Enhances macrophage, NK cell, and T-cell activity
Anti-inflammatory	Downregulates IL-1β, IL-6, TNF-α; inhibits COX-2 and iNOS pathways
Antioxidant	Scavenges free radicals; upregulates Nrf2 pathway
Gut microbiota modulation	Increases *Bifidobacterium*, *Lactobacillus*; suppresses pathogens like *E. coli*
Neuroprotection	Enhances cognition; protects neurons via anti-apoptotic signaling

2 MICROSPHERES

Microspheres are small spherical particles that typically range in diameter from 1 to 1000 micrometers. Microspheres are also known as microparticles or micro-particles. Microspheres can be made from both synthetic and natural materials. No biological waste is created because microspheres are biocompatible but not biodegradable. Protein entrapment inside biodegradable microspheres has garnered a lot of attention as a method to create protein formulations with prolonged release periods. PBT multi-block copolymers exhibit considerable potential as poly (lactide-co-glycolide) matrices for controlled release systems due to their exceptional biocompatibility and incorporation of non-therapeutically active proteins and peptides.[14-15]

2.1 Hydrogel Microsphere for colon Targeting disease

Probiotic drugs have the ability to prevent and treat a variety of illnesses by positively changing the balance of gut flora. We achieved synergistic therapeutic effects by co-delivering probiotics (Escherichia coli Nissle 1917, EcN) and auxiliary molecules (indole-3-propionic acid, IPA) utilizing droplet microfluidics to generate a hydrogel microsphere with mucoadhesive properties and colonic targeting. The integrated multifunctional microspheres have been shown in vivo to greatly reduce intestinal inflammation, restore intestinal barrier function, promote probiotic colonization within the intestine, and manage dysbiotic intestinal flora in a mouse model of colitis. This study demonstrates that microfluidics-based smart droplet microspheres offer a flexible platform for cutting-edge microbial therapies.

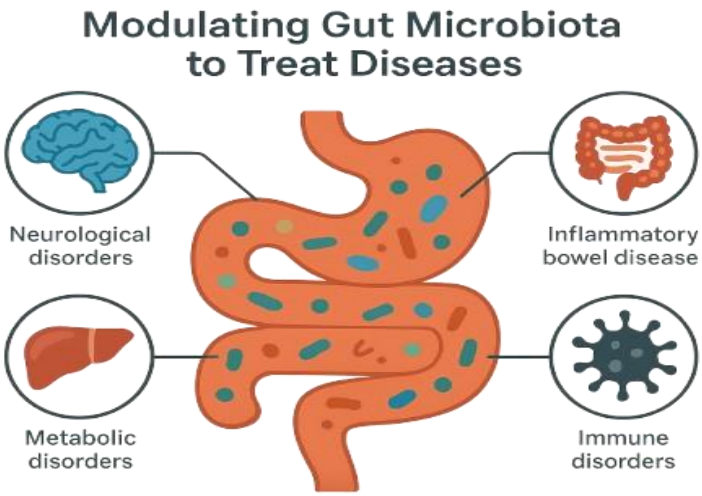

Figure: 3 Modulating gut microbiota to treat diseases.

This study presents a multifunctional probiotic delivery platform using a microfluidic-based encapsulation technique to modulate gut microbiota for disease treatment, as microfluidics has been widely used to create intelligent drug delivery systems through the preparation of microspheres with customizable size, shape, and functions.[16]

These microspheres are used to encapsulate and release medicinal components, such as drug molecules and living cells, under regulated conditions. More significantly, because of the segmented structure of the microspheres' adaptable architecture, this platform can co-deliver numerous therapeutic medications and auxiliary molecules, hence performing synergistic therapeutic functions. Furthermore, the way microspheres interact with biological tissues is directly related to their chemical moieties, which can be changed to improve their targeting and specialized adhesion abilities.[17] Therefore, the development of a multifunctional microsphere platform for the co-delivery of probiotics and auxiliary drugs, as well as disease-specific tissue interactions, may be made easier by microfluidics.[18,19]

All drug delivery systems aim to achieve the optimal concentrations of medication at a specific site within the body for a therapeutic effect. Without changing how quickly the stomach empties. Drugs with shorter half-lives and easy gastric absorption are swiftly eliminated from the bloodstream. These issues have led to the development of the oral controlled drug delivery system, which delivers the medication into the gastrointestinal tract for extended periods of time while maintaining a steady serum concentration of the drug. In addition to improving bioavailability, reducing drug waste, and increasing the solubility of

poorly soluble drugs, gastroretentive dosage forms can stay in the gastrointestinal tract for several hours, greatly extending the medication's gastric residence time (GRT).

Composed of free-moving particles that range in size from 1 to 1000 μm.[20, 21] Innovative drug delivery methods have a number of advantages over traditional multi-dose therapy. According to recent studies, microparticulate drug delivery methods are especially useful for oral formulations with regulated and delayed release, which reduce the possibility of dose dumping while providing blending flexibility to achieve various release patterns and ensuring consistent, short gastric residence times.[22]

These advanced drug delivery systems have the ability to target specific areas, change the rate at which medications are given, and extend the duration of treatment. Using microspheres as drug carriers is a highly advanced technique for maintaining and regulating pharmacological effects at particular sites.

Biodegradable microspheres are used for transient embolization. Theoretically, they should be eliminated from the body without affecting the function of other organs once their therapeutic objective has been met.[23]

Particulate delivery methods have garnered significant attention in the pharmaceutical sector due to their ability to control and target the release of active substances. This should, in theory, allow for the modification of drug release to satisfy therapeutic requirements.[24]

Predefined medication release profiles that satisfy the patient's therapeutic requirements can be provided. In order to increase the efficacy of various medical treatments, this article offers a comprehensive study of significant past, present, and future projects that use drug-loaded microparticles.[25]

Microparticles function as biological vectors that encourage coagulation and vascular inflammation by attaching to and integrating into target cells through receptor-ligand interactions. Microparticles have been demonstrated to have a major impact on a number of cardiovascular illnesses.

A growing body of research indicates that the pro-coagulant and inflammatory actions of microparticles on target cells are caused by their distinct lipid composition and the transfer of inflammatory cell components from their parent cells. While microparticles are useful for

delivering medications, They have little site-specificity and are normally rapidly eliminated by the reticuloendothelial system.[26]

Membrane vesicles have garnered significant attention in several scientific fields during the last decade, including vascular biology and thrombosis. Submicron membrane vesicles generated by living or dying cells are referred to as "microparticles" instead of "cell dust.".[27]

2.2 Ideal Characteristics of Microspheres[28-29]

Ability to control the release rate for a predefined period. Higher concentrations of the drug can be given to serve as a depot.

- Non-toxic.
- Relative stability
- Bioresorbability
- Increase therapeutic efficiency.
- Control of content release.
- Stability of the preparation after synthesis with a clinically acceptable shelf life.
- Biocompatibility with controllable biodegradability.
- Controlled particle size and dispersion of the drug in aqueous solvent for parenteral.
- Longer duration of action.
- Protect drug.

2.3 Limitation[30,31]

The modified release of the formulas. The release rate of the controlled release dose form can be influenced by a number of factors, including food and the rate of transit through the gut. Any modification to the dosage form's release characteristics could be dangerous since controlled release formulations frequently contain higher drug doses. It is not recommended to chew or crush such dose forms.

2.4 Materials Used In the Preparation of the Microsphere

Microspheres used usually are polymers. They are classified into two types.

Polymers Used in Hydrogel Microspheres for Gut Targeting[32]

The effectiveness of hydrogel microspheres for gut-targeted medication administration is largely dependent on the choice of polymers. Because of their biocompatibility,

biodegradability, and sensitivity to gastrointestinal environmental conditions, both natural and synthetic polymers are extensively studied.

1. Natural polymers
2. Synthetic Polymers

1. Natural polymers

Natural polymers come from a variety of sources, including proteins, carbohydrates, and chemically modified carbohydrates. Carbohydrates include things like agarose, carrageenan, chitosan, and starch; proteins include things like albumin, collagen, and chemically modified carbohydrates like polydextran and polystarch. Because of their non-toxicity, mucoadhesive qualities, and capacity for ionotropic gelation, substances such sodium alginate, chitosan, pectin, guar gum, and carrageenan are widely utilized. In particular, alginate exhibits pH-dependent swelling and forms stable hydrogels in the presence of divalent cations like calcium ions, making it appropriate for colon-specific administration.

2. Artificial polymers[33]

Poly (anhydrides), poly (alkyl cyanoacrylates), and biodegradable polymers, such as lactides, glycolides, and related copolymers, are the two types of synthetic polymers. Non-biodegradable polymers include acrolein, epoxy, glycidyl methacrylate, and polymethyl methacrylate.

Carbopol, Eudragit S100, and Eudragit L100 are widely used for pH-sensitive drug release. Eudragit S100 dissolves at pH levels higher than 7, allowing for targeted release in the colon and minimal medication release in the stomach and small intestine. Carbopol prolongs residence time at the site of action and improves mucoadhesion. Herbal bioactives frequently have better mechanical strength, controlled release behavior, and increased stability when natural and synthetic polymers are combined.

1.1.5 Methods of preparation

Numerous problems that come up when making pharmaceutical dosage forms can be resolved with these methods. Despite the difficulties in achieving continuous gastric retention, numerous businesses are attempting to commercialize this technology.[34] The microspheres were repeatedly cleaned with petroleum ether until no oil was left. The microspheres were collected, dried for an hour at room temperature, and then placed in desiccators with fused calcium chloride.[35]

- Single emulsion technique
- Double emulsion technique
- Polymerization
- Phase separation/ Coacervation

2.5 Formulation Techniques

1. the most used method for herbal microspheres is inotropic gelation

Mechanism: Upon dropping droplets of polymer-drug solution into a divalent cation solution (such as Ca2+), an instant gelation occurs.

Benefits: ideal for thermolabile bioactives, mild conditions, and absence of organic solvents. For instance, insoluble calcium alginate microspheres are created when sodium alginate and $CaCl_2$ are combined.

Steps

1. Dissolve the medication and polymer.
2. Stir to establish homogeneity.
3. Drop the solution into a calcium chloride bath using syringe or nozzle.
4. Harden for 20–30 min.
5. Filter, wash, and dry microspheres.

2. Emulsification–Crosslinking

- **Mechanism**: Polymer-drug aqueous solution is emulsified in oil (w/o) and then crosslinked chemically or thermally.
- **Used for**: Polymers like chitosan or gelatin.
- **Limitations**: Use of oil phase and toxic cross-linkers like glutaraldehyde may not suit herbal actives.

3. Spray-Drying

- **Mechanism**: Atomizes the drug-polymer solution into a hot chamber where rapid solvent evaporation forms microspheres.
- **Advantages**: Scalable, produces dry powder.
- **Limitations**: Not ideal for thermolabile phytochemicals due to high temperatures.

4. Solvent Evaporation

- **Mechanism**: Drug-polymer solution is emulsified in an immiscible solvent, and the solvent is evaporated under reduced pressure.
- **Suitable for**: Hydrophobic drugs with polymers like Eudragit.
- **Limitations**: Less effective for highly water-soluble herbal extracts.

2.6 Precise Modulation of Gut Microbiome via Pharmacological Delivery

The human gut microbiota is essential for immune regulation, food metabolism, and pathogen resistance. Changing its composition through targeted pharmaceutical administration is a promising treatment approach for neurological disorders, obesity, and inflammatory bowel disease (IBD). Colon-targeted delivery techniques are essential for permitting localized release of bioactives in the colon, where the bulk of gut bacteria are present. However, proper distribution is hampered by a number of factors in the gastrointestinal (GI) tract, such as the mucus layer, digestive enzymes, pH fluctuations, and rapid transit time.

Temporally-responsive and pH-sensitive polymeric systems have been developed to solve these problems. Since polymers like Eudragit S100 only degrade at the high pH of the colon (~pH 7), they guarantee restricted drug release in the stomach or small intestine. Similarly, time-dependent techniques use hydrophilic polymers to delay the release of medications until they reach the colon. Ginsenosides, bioactive compounds produced from Panax quinquefolius (American ginseng), have prebiotic and immunomodulatory properties that make their integration into different delivery methods particularly attractive. When ginsenosides are released into the colon, they can have a positive impact on the gut microbiota by reducing pro-inflammatory species and encouraging the growth of beneficial bacteria like Lactobacillus and Bifidobacterium. Future therapeutic approaches could greatly benefit from medicine delivery's dual function of safeguarding the payload and facilitating microbiome-targeted release.[36, 37]

Clinical Relevance and Therapeutic Implications

Panax quinquefolius-loaded hydrogel microspheres can be used to target the gut microbiota, which has important clinical implications for the treatment of systemic and gastrointestinal illnesses. Inflammatory bowel illness, irritable bowel syndrome, metabolic syndrome, obesity, neuroinflammatory diseases, and colorectal cancer have all been linked to dysbiosis of the gut microbiota. Ginsenosides' colon-specific release allows for targeted therapeutic action, reducing systemic side effects and improving treatment effectiveness.

Hydrogel microspheres shield ginsenosides from stomach breakdown and enable long-term contact with intestinal microbiota, which encourages the growth of beneficial bacteria and the synthesis of short-chain fatty acids. Particularly in chronic illnesses requiring long-term treatment, this administration method offers a promising supplement or substitute for traditional medication.[38,39]

2.7 Assessment of Hydrogel Microspheres

A thorough pharmaceutical study is required to ensure that hydrogel microspheres meet quality, safety, and efficacy standards. Particle size and surface morphology are frequently measured using scanning electron microscopy (SEM), which creates high-resolution images for evaluating the homogeneity, surface smoothness, and shape of microspheres. The swelling index is determined by submerging microspheres in physiological fluids and measuring the rise in weight or diameter, which reveals their responsiveness and water absorption capacity and influences drug release.[40]

When the drug is extracted from a particular weight of microspheres, spectrophotometry measures the crucial statistic known as drug entrapment efficiency (DEE). A high Drug Encapsulation Efficiency (DEE) indicates effective drug incorporation into the polymeric matrix. Mucoadhesion studies evaluate the ability of microspheres to adhere to mucosal surfaces, which is essential for enhancing localized administration and prolonging the duration of gastrointestinal residency. For this, mucin-coated glass slides or models of excised intestinal tissue are frequently utilized. In vitro drug release studies are conducted using artificial stomach fluid (pH 1.2), intestinal fluid (pH 6.8), and colonic fluid (pH 7.4) to mimic physiological transit conditions.[41]

These enable the identification of site-specific release patterns and demonstrate the impact of pH on drug release. Fourier Transform Infrared Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC) are used to assess drug-polymer compatibility. FTIR indicates possible chemical interactions, whereas DSC finds changes in the drug's melting point or thermal behavior, indicating physical or chemical incompatibility. To evaluate shelf-life, stability tests are carried out under accelerated settings (e.g., $40 \pm 2°C$ / $75 \pm 5\%$ RH) for several months, analyzing characteristics including drug content, morphology, and release behavior over time. When combined, these techniques offer a thorough evaluation of the efficacy and quality of hydrogel microspheres.[42]

Limitation

There are still some issues with Panax quinquefolius-loaded hydrogel microspheres, notwithstanding their potential for gut-targeted delivery. First, most of the current information is derived from in vitro studies, which are unable to replicate the complex physiological environment of the human gastrointestinal tract. Variables including varying pH, enzyme activity, mucus turnover, and intestinal motility may alter the actual drug release and mucoadhesion performance in vivo. Second, the duration of ginsenosides' stability in the hydrogel matrix is still unknown, and degradation may reduce their therapeutic efficacy.

Because the preparation method might impact encapsulation efficiency and uniform particle size distribution, large-scale manufacturing is challenging. Another disadvantage is the lack of clinical and animal studies confirming the microbiome-modulating effects predicted in laboratory studies. The interaction of hydrogel materials with the gut flora may also affect site-specific release, potentially leading to unpredictable biotransformation or early destruction. Furthermore, regulatory approval, biocompatibility, and repeatability may be impacted by batch-to-batch variability caused by the use of natural polymers. Overall, despite the formulation's intriguing approach, these limitations highlight the need for further comprehensive mechanistic, preclinical, and clinical study.[43]

CONCLUSION

The potential of hydrogel microspheres as a cutting-edge and efficient platform for the gut-targeted administration of Panax quinquefolius L. bioactives is highlighted in this research. These methods improve the stability, bioavailability, and site-specific release of ginsenosides by getting past the physiological barriers of the gastrointestinal tract. A synergistic strategy for accurate gut microbiota regulation is provided by the combination of polymer-based delivery methods and herbal remedies. All things considered, hydrogel microspheres loaded with Panax quinquefolius offer a potential approach to treating illnesses linked to the microbiota. To confirm their therapeutic efficacy and make it easier to translate them into practical applications, more in vivo and clinical research is needed.

REFERENCES

1. Turnbaugh, P. J., Ley, R. E., Hamady, M., Fraser-Liggett, C. M., Knight, R., & Gordon, J. I. (2007). The human microbiome project. *Nature, 449*(7164): 804–810. https://doi.org/10.1038/nature06244.
2. Lynch, S. V., & Pedersen, O. (2016). The human intestinal microbiome in health and disease. *New England Journal of Medicine, 375*(24): 2369–2379. https://doi.org/10.1056/NEJMra1600266
3. Aulton M.E. Pharmaceutics The science of dosage form design. Second ed, Churchill Livingstone; 2004.
4. Piyakulawat Pimwipha, Praphairaksit Nalena, Chantarasiri Nuanphun, Muangsin Nongnuj. Preparation and Evaluation of Chitosan/Carrageenan beads for Controlled release of Sodium Diclofenac. AAPS PharmSciTech, 2007; 8(4): Article 97: E1 – E10.
5. Ursell, L. K. et al. The intestinal metabolome: an intersection between microbiota and host. Gastroenterology, 2014; 146: 1470–1476.
6. Grice, E. A. & Segre, J. A. The human microbiome: our second genome. Annu. Rev. Genom. Hum. Genet, 2012; 13: 151–170.
7. Berg, G. et al. Microbiome definition re-visited: old concepts and new challenges. Microbiome, 2020; 8: 103.
8. Shreiner, A. B., Kao, J. Y. & Young, V. B. The gut microbiome in health and in disease. Curr. Opin. Gastroenterol, 2015; 31: 69–75.
9. Kho ZY, Lal SK**.** The human gut microbiome – A potential controller of wellness and disease. *Front Microbiol*, 2018; 9: 1835. doi:10.3389/fmicb.2018.01835
10. Shreiner AB, Kao JY, Young VB. The gut microbiome in health and in disease. *Curr Opin Gastroenterol*, 2015; 31(1): 69-75. doi:10.1097/MOG.0000000000000139
11. Huang HP, Ghebre-Sellassie I. Preparation of microspheres of water-soluble pharmaceuticals. J Microencapsul, 1989; 6(2): 219–25.
12. Sinha, V. R., Kumria, R., & Bhinge, J. R. (2007). Polysaccharides in colon-specific drug delivery. *International Journal of Pharmaceutics, 224*(1–2): 19–38. https://doi.org/10.1016/S0378-5173(01)00720-7
13. Philip, A. K., & Philip, B. (2010). Colon targeted drug delivery systems: A review on primary and novel approaches. *Oman Medical Journal, 25*(2): 79–87. https://doi.org/10.5001/omj.2010.24

14. Hussein, H. A., and Abdullah, M. A. (2021). Novel drug delivery systems based on silver nanoparticles, hyaluronic acid, lipid nanoparticles and liposomes for cancer treatment. Appl. Nano, 1–26. doi: 10.1007/s13204-021-02018-9.
15. Alam S, Hasan K, Neaz S, Hussain N, Hossain F. Diabetes mellitus : Insights from epidemiology, biochemistry, risk factors, diagnosis, complications and comprehensive management. Diabetology, 2021; 2(2): 36–50.
16. Ta.S. Diagnosis and classification of diabetes mellitus. Diabetes Care, 2014; 37(1): 81–90.
17. Ohiagu FO, Chikezie PC, Chikezie CM. Pathophysiology of diabetes mellitus complications: Metabolic events and control. Biomed Res Ther, 2021; 8(3): 4243–57. and biodegradation, 13.
18. Mirmeera GN, Kannan K, Madhukar. A Overview on Floating drug delivery system. International Journal of Applied Pharmaceutics, 2018; 10(6): 66-70.
19. Lalit K, Abhishek S. Gastro Retentive Floating Microsphere: A Review. Journal of Pharmaceutical Sciences & Bioscientific Research, 2019; 9(2): 142-148.
20. Shinde TS, Barathe AN. A Review on Floating Microsphere. Journal of Pharmaceutical and Biological Sciences Archive, 2019; 7(3): 87-92. Radha R, Manish.
21. Poovi Ganesan, Arul Jasmine Deepa Johnson LS and AD. Review on microsphere. Am J drug Discov Dev, 2014; 4(3): 1–28.
22. Vaibhav R, Satya SS, Roop S, Lal N, Pragya Y. Review Article Microspheres : a Promising Drug Carrier. J Drug Deliv Ther, 2016; 6: 18–26.
23. Doucet J, Kiri L, Connell KO, Kehoe S, Lewandowski RJ, Liu DM, et al. Advances in degradable embolic microspheres: A state of the art review. J Funct Biomater Rev, 2018; 9(14): 1–24.
24. Scalia S, Young PM, Traini D. Solid lipid microparticles as an approach to drug delivery. Expert Opin Drug Deliv, 2014; 12(5): 1–17.
25. Juergen Siepmann FS. Microparticles used as drug delivery systems. Progr Colloid Polym Sci, 2006; 133: 15–21.
26. Diehl P, Fricke A, Sander L, Stamm J, Bassler N, Htun N, et al. Microparticles: Major transport vehicles for distinct micro RNAs in circulation. Cardiovasc Res, 2012; 93(4): 633–44.
27. Momoh MA, Kenechukwu FC, Attama AA. Formulation and evaluation of novel solid lipid microparticles as a sustained release system for the delivery of metformin hydrochloride. Inf Healthc, 2013; 20(3): 102–11.

28. Boulanger CM, Dignat-George F, Boulanger CM. Microparticles : An introduction. Arter Thromb Vasc Biol, 2011; 31(1): 2–3.
29. Lee DW, Hwang SJ, Park JB, Park HJ. Preparation and release characteristics of polymer-coated and blended alginate microspheres. J Microencapsul, 2003; 20(2): 179–92.
30. Li X, Wei Y, Lv P, Wu Y, Ogino K, Ma G. Preparation of ropivacaine loaded PLGA microspheres as controlled-release system with narrow size distribution and high loading efficiency. Colloids Surfaces A Physicochem Eng Asp, 2019; 562: 237–46.
31. Wang X, Wang X, Liu L, Bai L, An H, Zheng L, et al. Preparation and characterization of carbon aerogel microspheres by an inverse emulsion polymerization. J Non Cryst Solids, 2011; 357(3): 793–7.
32. Anal, A. K., & Singh, H. (2007). Recent advances in microencapsulation of probiotics for industrial applications. *Trends in Food Science & Technology, 18*(5): 240–251. https://doi.org/10.1016/j.tifs.2007.01.007
33. George, M., & Abraham, T. E. (2006). Polyionic hydrocolloids for the intestinal delivery of protein drugs: Alginate and chitosan. *Journal of Controlled Release, 114*(1): 1–14. https://doi.org/10.1016/j.jconrel.2006.04.017
34. Katz LC, Iarovici DM. Green fluorescent latex microspheres: A new retrograde tracer. Neuroscience, 1990; 34(2): 511–20.
35. Patil S, Sawant K. Mucoadhesive microspheres: A promising tool in Drug Delivery. Curr Drug Deliv, 2008; 5(4): 312–8.
36. Yang X, Flynn R, Von Der Kammer F, Hofmann T. Influence of ionic strength and pH on the limitation of latex microsphere deposition sites on iron-oxide coated sand by humic acid. Environ Pollut, 2011; 159(7): 1896–904.
37. C. Singh; S. Purohit; M. Singh; B. L. Pandey. Design and evaluation of microspheres : A review. J Drug Deliv Res, 2013; 2(2): 18–27.
38. Zhou, W., & Liu, Y. (2006).“Extraction and analysis of ginsenosides from *Panax quinquefolium* L.” *Journal of Pharmaceutical and Biomedical Analysis*, 40(3): 713–719.
39. Yang, X., Nie, W., Wang, C., Fang, Z., & Shang, L. (2024). Microfluidic-based multifunctional microspheres for enhanced oral co-delivery of probiotics and postbiotics. Biomaterials, 308: 122564.
40. Peterson, L. W., & Artis, D. (2014). Intestinal epithelial cells: Regulators of barrier function and immune homeostasis. *Nature Reviews Immunology*, 14(3): 141–153. https://doi.org/10.1038/nri3608

41. Choi, J. S., & Youn, Y. S. (2012). Colon-targeted delivery of ginsenosides for modulation of gut microbiota: Current advances and future perspectives. *Journal of Ginseng Research*, 36(3): 239–247.
42. Nafee, N., Boraie, N., Ismail, F., & Mortada, L. (2005). Design and characterization of mucoadhesive buccal patches containing cetylpyridinium chloride. *Acta Pharmaceutica*, **55**(3): 255–266. https://doi.org/10.2478/v10007-005-0033-0
43. Soppimath, K. S., Kulkarni, A. R., Rudzinski, W. E., & Aminabhavi, T. M. (2001). Microspheres as floating drug-delivery systems to increase gastric retention of drugs. *Drug Metabolism Reviews*, 33(2): 149–160.