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Biodegradable Polymers in Herbal Formulations

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Abstract:

The development of herbal formulations with biodegradable polymers has developed into a potentially useful method of improving the pharmacodynamic potency, bioavailability and patient compliance of herbal medicines (1). Herbal drugs find wide applications in both traditional and contemporary healthcare systems, but present many problems that include poor solubility, instability, and low absorption, and uncontrolled-release (13). Biodegradable polymers provide a renewable and biocompatible system to overcome these drawbacks, and confer release control, targeting and enhanced stability of biologically active phytoconstituents (19). This review article has addressed the taxonomies of biodegradable polymers, both natural (chitosan, alginate, starch, gelatin) and synthetic (poly(lactic acid), poly(lactic-co-glycolic acid), polycaprolactone) and their vuses in novel herb delivery systems using nanoparticles, microspheres, hydrogels, and scaffolds (22). In addition, the review discusses recent developments, current knowledge, constraints, regulations and future of the field of herbal therapeutics based on polymers. The end goal is to give an extensive account of the possibility of the biodegradable polymers in the field of delivering a wide gap between conventional herbal drugs as compared to present-day innovations in the technological sectors in pharmaceuticals that make a huge difference concerning innovation in drug delivery science.

Keywords: Biodegradable polymers, herbal formulation, delivery of drugs, nanoparticles, controlled release, phytoconstituents

1. Introduction

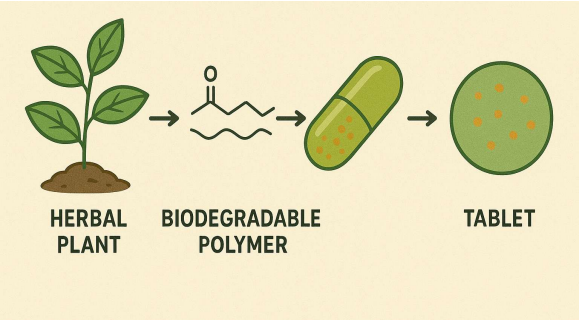
In ancient times, herbal drug was the base of healthcare, and further than 80 percent of the population in the world depends on plants and plant derivatives to treat primary health situations, particularly World Health Organization(2021). It has been reported that phytoconstituents(alkaloids, flavonoids, terpenoids, tannins and saponins) retain a variety of pharmacological conditioning similar as anti-inflammatory, antioxidant, anticancer, antimicrobial, and hepatoprotective effects . Possible regulation of bioavailability, rapid-fire metabolism, lack of waterless solubility, poor bioavailability and insecurity to chemicals is a factor that substantially limits the use of herbal medicines despite their remedial eventuality. These limitations make them less applicable to the clinical setting and decrease patient adherence (Patel et al., 2020).(1)

To remedy them, scientists have resorted to the advanced drug delivery systems (DDS), which can substantially protect, deliver, and regulate the herbal actives/release. Of these, particularly immense attention is given to bio

degradable polymers owing to their capability to disintegrate in the body naturally to non-toxic products. These polymers have the ability to protect, or shield, sensitive phytoconstituents by preventing their degradation and allowing their controlled or targeted release to a required site of action (Singh & Sharma, 2019).(13)

The various types of polymers have different strengths and weaknesses whenconcerning bio-degradation rate, strength, drug delivery and compatibility with herbal actives. The materials are diverse to fit a range of drug delivery vehicles such as nanoparticles, microspheres, hydrogels, and scaffolds rendering them unique drug delivery platforms that can be used in the development of herbal formulations.(19)

Polymer-based herbal drug delivery systems have been explored in the last several years with many herbal bioactives, including curcumin, quercetin, resveratrol, ashwagandha and neem. These formulations have demonstrated better solubility, stability and bioavailability than conventional dosage forms of herbals (22)



- **Biodegradable polymers used in herbal formulations**

Polymer	Source	Biodegradable mechanism	Applications in herbal formulations	Examples
Chitosan	Natural	Enzymatic degradation of chitosananase	Controlled release of herbal extracts	Curcumin
Alginate	Seaweed	Ion exchange & enzymatic hydrolysis	Encapsulation of herbal actives	Neem
Gelatin	Collagen	Proteolytic enzymes	Herbal wound dressing	Ashwagandha
Poly(lactic acid)(PLA)	Synthetic (fermentation of sugar/strach)	Hydrolytic degradation to lactic acid	Nano particles for herbal drug delivery	Grean tea
Poly- (lactic-co-glycolic acid), (PLGA)	Synthetic	Hydrolytic to glycolic acid and lactic acid	Sustained release herbal microspheres	Curcumin
Strach based polymers	Natural	Enzymatic hydrolysis by amylase	Herbal tablet binders and films	Antioxidants
Cellulose derivatives (HMPC, CMC)	Natural	Enzymatic and microbial degradation	Coatings, matrix tablets	Herbal tablets

Pectin	**Plant cell walls**	**Microbial and enzymatic degradation in colon**	**Hydrogels**	**Aloevera gel**

2. Biodegradable Polymers An overview

Biodegradable polymers refer to those macromolecules that degrade in the presence of the body through enzymatic or non-enzymatic routes, to be ultimately reduced to biocompatible and non-toxic products that may include carbon dioxide, water, and natural metabolites (Ahuja et al., 2019). (1)Their biodegradation profile will also find use in the pharmaceutical application, as long term deposition of non-degradable carriers may cause toxicity.(9)

Biodegradable polymers are materials able of witnessing degradation intonon-toxic, low- molecular- weight products through natural processes similar as enzymatic action, hydrolysis, or microbial metabolism. Due to their biocompatibility and environmentally friendly nature, these polymers have gained significant significance in pharmaceutical sciences, particularly in medicine delivery and biomedical operations(1).

In drug delivery systems, biodegradable polymers serve as carriers that cover remedial agents from degradation and improves their stability. Upon administration, these polymers gradually degrade into harmless products, enabling controlled medicine release and minimizing the need for surgical junking after therapy(2).

Biodegradable polymers may be of the following types:

Natural polymers such as plant, animal or microbial.Chemically manufactured and customized polymers synthetic polymers. Examples: PLA, PLGA, PCL and polyanhydrides.Semi-synthetic polymers- natural polymers that are chemically modified in order to optimize performance.

Drug Delivery Properties Needed:

A biodegradable polymer to be used in herbal formulations:Be nontoxic, biocompatible.Have controlled kinetics of degradation.Be mechanically stable.Be able to tolerate high drug loading, efficiency of entrapment.The biodegradation is via a hydrolytic cleavage, an action of the enzyme, or in combination. Natural polymers may be easily broken down by the activity of enzymes, whereas the main mechanism used in the degradation of synthetic polymers, such as PLGA, is the hydrolysis of ester bonds(19) The rate of degradation can be optimized with change in polymer, molecular weight and crystallinity of the polymer and thus determines the pattern of drug release.

3. Herbal natural biodegradable polymers

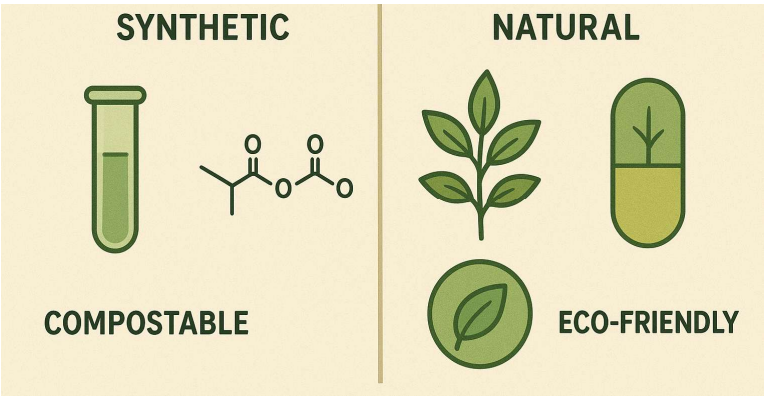
- Chitosan.
  Chitin can be extracted to form a cationic polysaccharide chitosan, which has received a lot of research on herbal drug delivery. It is biocompatible, mucoadhesive and increases permeability of poorly absorbed orally administered herbal constituents. Chitosan nanoparticles have also been applied to the delivery of curcumin, quercetin, and resveratrol enhancing the bioavailability and stability (Sogias et al., 2020).(20)
- Alginate
  Alginates, polysaccharide extracted by the brown algae, produce hydro-gels under the influence of a supply of divalent cations, such as calcium. Herbal extracts like neem and aloe vera have also been found

to encapsulate in alginate-based beads and microspheres, which showed controlled release as well as gastric degradation protection (George & Abraham, 2020).(7)

- Starch and Derivatives
  Starch is rich and biodegradable, and starch derivatives (crosslinked, hydroxy-propylated) can also enhance entrapment and release characteristics of drugs. Antioxidants such as catechins and herbal polyphenols have been encapsulated with starch nanoparticles (Prasad et al., 2021).(15)
- Gelatin
  Collagen is a protein that can be found as hydrogel and microspheres. It offers significant biocompatibility and is acceptable in the encapsulation of the hydrophilic and hydrophobic herbal actives. As an example, gelatin nanoparticles with loaded curcumin have demonstrated the augmentation of anticancer activity (Patra et al., 2019).(14)
- Guar Gum, Pectin, and others
  Guar gum or pectin-type polysaccharides-Gauar gum and pectin-type polysaccharides are commonly used in colon-targeted drug delivery of herbs. Such polymers are stable in the upper gastrointestinal tract but are vulnerable to colon microflora hence, they are appropriate carriers of herbal extracts to treat colonic disorders (Mishra et al., 2020).(11)

4. Synthetic Biodegradable Polymers in the Herbal Formulations

- Polylactic Acid (PLA)
  LA is a synthetic aliphatic polyester with very high biocompatibility and biodegradability. The use of PLA nanoparticles in the entrapment of poorly-soluble natural products has also been applied to curcumin and resveratrol (21)
- Plga - Polylactic-co-glycolic acid
  LGA nanoparticles have been exploited as herbal formulations of quercetin, catechins, and silymarin in a controlled direct manner (5)
- Polycaprolactone (PCL)
  PCL is a biodegradable polymer with slow degradation that can be utilized in long-term release applications.PCL microspheres of herbal extracts such as curcumin and neem have been produced to serve anticancer and antimicrobial therapy (10)
- Polyanhydrides and Others
  They are used in the form of herbal preparations that demand a linear release profile (4)



5. Herbal Drug Delivery Systems using Polymers.

Nanoparticles

Nanoparticles offers a high surface area to volume ratio that can increase the solubility and bioavailability of lowly soluble plants. These include chitosan-curcumin nanoparticles and PLGA-quercetin nanoparticles with a better pharmacological effect.(8)

Microspheres

Ashwagandha extract has also been encapsulated in alginate-gelatin microspheres to form a prolonged effect . (12)

Hydro gels

Pectin and chitosan-based herbal hydrogels have been investigated as wound healing agents as they form a moist environment and release herbal actives, such as aloe vera and neem over a period of time. (16)

Scaffolds and Films

Topical topical use of herbs in wound healing and tissue engineering On such scaffolds or films; dermal or topical delivery is guided by the direction of the top. A case in point is the chitosan-aloe vera composite films that are documented to exhibit antibacterial and regenerative effects. (18)

Colon- Targeted Polymeric Systems

Polymers derived from plant polysaccharides are resistant to digestion in the upper gastrointestinal tract but are degraded by colonic microflora. This property is exploited for colon- targeted delivery of herbal medicines, improves therapeutic outcomes in bowel diseases and colorectal diseases(11).

6. The Applications of the Biodegradable Polymers in Herbal Formulations

1. Enhancing solubility and absorption

The ability of herbal bioactive compounds to be absorbed will often suffer from poor solubility and therefore limits to some extent the ability to absorb the compounds into the body, which in turn, limits their therapeutic potential. By using biodegradable polymers (e.g.: PLGA, chitosan, gelatin), phytoconstituents can have improved aqueous solubility while also protecting them from degradation by enzymes within the GI tract (5). Enhanced polymer-drug interactions can also result in an improved rate of dissolution and permeation across the intestinal wall of herbal drugs (10).

2. Controlled and sustained release of herbal drugs

The sustained delivery of herbal drugs can be achieved through the gradual degradation of biodegradable polymers, either by means of polymer erosion or via diffusion-controlled mechanisms. Biodegradable polymeric materials (e.g.: polyanhydrides and PLGA) have been shown to sustain the delivery of a therapeutic concentration of drugs for extended periods, decreasing the frequency of dosing and thereby increasing the effectiveness of treatment (4). Additionally, the prolonged delivery provided by polymeric microspheres is of great value in the treatment of chronic conditions with herbal biomaterials (12).

3. Targeted Delivery of Herbal Drug Formulations

Targeted delivery of herbal drugs will provide therapeutic benefits to patients. Natural polymers can be derived from plants and are indigestible in the upper GI tract, but degrade selectively in the colon. This means that these natural polymeric materials can therefore be used to deliver herbal drugs to the colon (11), which is desirable for treating patients with inflammatory bowel disease and other colon-related conditions (16).

4. Improved Safety and Patient Compliance

The degradation of biodegradable polymers into non-toxic metabolites leads to a significant reduction in both systemic toxicity and long-term safety concerns regarding the use of these materials. In addition, the biocompatibility of these polymers, along with their ability to provide sustained release of medication, increases the levels of patient compliance and therapeutic reliability in using herbal medicines (1). Lastly, the use of polymeric nanocarriers helps to reduce the amount of variability associated with the traditional means of preparing herbal products (24).

7. Challenges and Future Prospects

Although great progress is being made, there are a few obstacles in the way of commercializing biodegradable polymer-based herbal formulations:

Toxicity and safety: Despite being safe in general, lack of proper choice of a polymer or residual solvents may result in toxicity. (9)

Stability problems: The herbal extracts are chemically complicated and there can be a problem of interactions of polymers and influence on stability. (23)

Scale-up problems Laboratory manufactures of formulas are not always easily scaled up into industrial manufactures. (24)

Regulatory impediments The herbal- polymer formulations don't have designated nonsupervisory instructions, thus decelerating the process of gaining blessing in the request.

Future outlook:Smart polymer development pH-, temperature- or enzyme-responsive polymers to deliver herb to specific sites.

Herbal multifunction formulation with nanotechnology and biotechnology. (23)

8. Conclusion

Herbal drugs have several disadvantages, e.g. low solubility, instability, and swift metabolism, which have been overcome with the use of both natural and synthetic polymers. (1). The flexibility of the biodegradable polymers allows the formulation of nanoparticles, microspheres, hydrogels and scaffolds with controlled and targeted delivery platforms. (19). Although issues with toxicity, scale, and regulation have yet to be solved, future work has a lot of promise in terms of polymer-based herbal treatment. (22). The combination of biodegradable polymers with herbal medicine is a synthesis of modernity with traditional care and this leads to an opportunity to have safer, effective, and patient friendly therapeutic options.(1). Deposition of herbal bioactives in bio-degradable polymeric based systems has also shown high level of interference in terms of therapeutic performance. Polymeric

carrier system through encapsulation achieves improved absorption and prolonged circulation to the target site tissue, in addition to protecting sensitive phytoconstituents to environmental and physiological degradation. (19). In addition, biodegradable polymers can be used in diverse ways to deliver herbal medicine, such as via oral, transdermal, mucosal, and parenteral systems to further expand the formulation approach to herbal drug delivery. Therefore there is a new enabling factor in the modernisation and globalisation of herbal therapeutics; biodegradable polymers.(1)

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