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Review paper

A review on evaluation of natural polymers with the approach of drug delivery system using herbal plant microcapsules

Amirreza Esmaeili[1]*, Romina Hemami[2]**, Yashar Ghaffari[3], Somayeh Abdollahi[4]

[1]*Plant Protection Faculty of Agriculture, Shahrekord University, Chaharmahal and Bakhtiari, Iran*
[2]*Faculty of Pharmaceutical Chemistry, Azad University of Medical Sciences, Tehran Branch, Tehran, Iran*
[3]*Department of Biomedical Engineering, Science and Research Branch, Islamic Azad University, Tehran, Iran*
[4]*Department of biomedical engineering Isfahan (Khorasgon) Branch, Islamic Azad University, Isfahan, Iran*

*amirrezaesmaeili75@yahoo.com, **rominahemmami@gmail.com

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Abstract

Drug release in the body, mainly by digestive (tablets, capsules, and syrups) and non-digestive (injections, eye drops, and creams) are known as conventional technique. In most of these methods, the drug travels through the body during exposure to the acidic environment of the stomach, passing through the tight connections of cells in the intestinal wall. This attitude is based on the fact that a sufficient concentration of the drug enters the bloodstream. The process of targeted drug delivery maintains the level of an appropriate drug concentrations for a long time and reduces many of the usual therapeutic limitations such as the number of doses used. In this research, the use of natural biopolymers in the engineering and medical engineering industries and the use of electro spraying for core-shell have been investigated. Also, the side effects of simple drug release in the systemic distribution are unclear. Each targeted delivery system includes a target drug, carrier, and ligand, in which the distribution, metabolism, and cellular uptake of the drug are determined by the physicochemical characteristics and biological behavior of the carrier and ligand. Therefore, proper carrier and ligand design increases drug efficacy in patient tissues and reduces drug toxicity in other healthy tissues. Many new techniques such as electrospray using natural polymers can use for treatment of those disease with sufficient time of drug release using an appropriate drug.

Keywords: Drug release, Mechanical properties, Polymer, Chitosan, Herbal medicine

1- Introduction

Drug release systems are systems used to improve the therapeutic effects and reduce the drugs side effects [1-4]. For example, the placement of drugs in capsules to protect them against acidic conditions and gastric enzymes is one of the drug delivery systems applications [4-6]. Nanomaterials are chemicals produced without changing the main mechanical and chemical properties, such as increasing the strength of the chemical reaction or the ability to conduct on a very small scale [7-9]. The development and production of biopolymers in medicine is increasing in the third millennium. Polymeric materials have many applications in drug delivery due to their unique properties such as biocompatibility and biodegradability. Thus, the polymers on the one hand protect the active drug compound on the other hand the possibility of targeting. Controlled drug delivery provides predictable drug delivery after administration, either topically or systemically [10-14].

The mechanical properties of natural polymers are usually weaker than industrial materials and a number of synthetic polymers, and this issue limits the industrial applications of these materials. To predict and measure the mechanical properties of these types of polymers some methods are usually applied such as molecular dynamic simulation methods. Also, new production methods or combining these materials with other materials are used to make nanocomposites to increase their mechanical properties, including mechanical strength and elastic modulus. One of the fields of development of natural polymers in biomechanical applications is the use of these materials in some new production methods such as 3D printers. Polymers are widely used as active agents in various matrix, layered and film forms in drug delivery, in this case, they can control the release of the drug in the long-term preventing its repeated usage. They can also be used as drug carriers, especially for insoluble drugs.

2-Natural and synthetic polymers

There are several categories for polymers that can be divided into natural and synthetic or biodegradable and non-biodegradable as shown in Fig. 1. Synthetic polymers are polymers that are not obtained from nature and are made in the laboratory with synthesis process. Polyethylene glycol, polycaprolactone (PCL), polyglycolic acid (PGA) and polylactic acid (PLA) are examples of these polymers [22-25]. In biological applications, natural polymers seem to be the first choice, because they have good biocompatibility and unique mechanical properties. These polymers are also biodegradable by enzymatic mechanisms or hydrolysis. Another advantage of natural polymers is their availability, cost-effectiveness, solubility in water, ability to form hydrogels, their wide structure and properties [14-21]. In addition, most natural polymers can be easily modified because there are active groups in their polymer chains. Natural polymers are more biologically compatible than synthetic polymers due to their extracellular components (ECM), which contain specific Arg-Gly-Asp cell domains. Natural polymers are mainly in three categories of plant sources (cellulose (bacterial), silk, and chitosan.

Polymers can be in various forms, including hydrogels and scaffold. Whenever the solvent is in the gel network, water or aqueous solutions, the gel is called a hydrogel. Unlike other implantable systems that are hydrophobic, this material has hydrophilic properties and has received much attention due to its various properties such as biodegradability, biocompatibility, acceptable mechanical properties and adsorption capacity. A hydrogel is a three-dimensional (3D) hydrophilic network that has many applications in medicine, including drug release, scaffolding (their structure is similar to the extracellular matrix of many tissues), biosensors, and

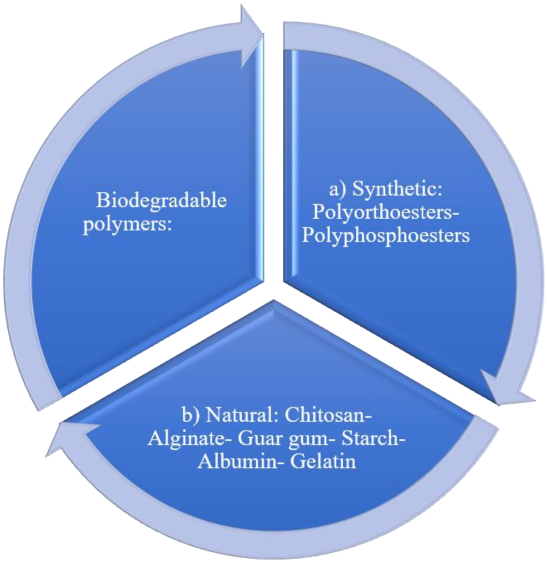

Fig. 1 Biodegradable polymers as synthetic and natural polymers

contact lenses. Multi-drug release properties, reducing resistance to drug release, reducing the likelihood of metastasis are some of the benefits of using this structure. Implantation of this type of hydrogel can largely prevent tumor recurrence and metastasis.

Chitosan is obtained from the distillation of catechins, which are natural, hydrophilic, non-toxic, environmentally friendly and biodegradable. Polysaccharide is suitable for use in pharmaceutical technology which has been studied in drug delivery systems (DDS) due to its chemical and biological properties. Chitosan is a branched homopolymer composed of glucosamine units by β- (1,4) bonds. Hydroxyl and its amine group are substrates for chemical modifications to obtain suitable materials for different purposes. A mucosal adhesion formulation is being developed that is used to prescribe medication through the eye, respiratory tract, oral cavity, and gastrointestinal tract.

Fig. 2 shows the mechanical properties of natural polymers such as stiffness and elastic modulus which influence on their

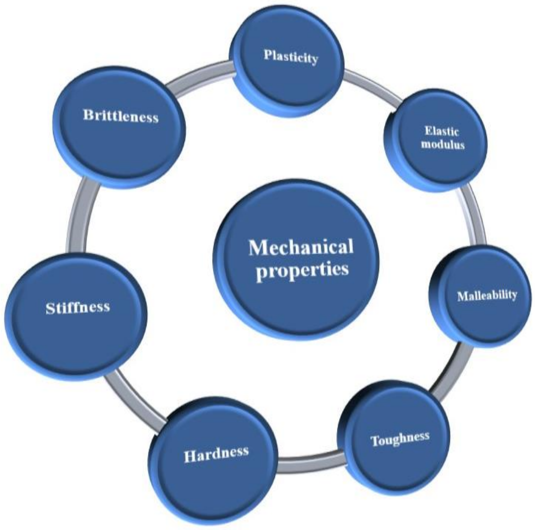

Fig. 2 Mechanical properties of natural polymers for use in the core-shell process

behaviors. Due to the nature of the chitosan polymer, it has been widely used in the pharmaceutical and mechanical industry for membrane and catalyst applications. Chitosan is also a candidate for potent applications in radiopharmaceuticals, genes and peptides for drug delivery. Today, chemical and biochemical methods are being developed with lots of interest for mechanical engineers. Processes for obtaining and modifying biopolymers are useful techniques for application in various fields. Chitin, poly-β- (1-4) -N-acetyl-D-glucosamine is one of the most important natural polysaccharides, first identified in 1884. Chitin is the most abundant natural biopolymer after cellulose, which is made by many living organisms. The natural properties of chitin are in the form of crystalline microfibers, which are the structural components of the exoskeleton of arthropods and the cell wall of fungi and yeasts. The chitosan polymer is the result of the removal of acetyl groups in chitin. Unlike most natural polysaccharides such as cellulose, dextran and agarose, which are acidic in nature. The percentage of nitrogen in chitin, depending on the degree of deacetylation, is between 5-8%, but nitrogen in chitosan is often present in the form of the first type of amine. Molecular weight and degree of acetylation are characteristics. Drug delivery systems can be different from different aspects, including drug delivery path, system appearance, type of drug available categorized in the system as well as the target context.

3-Microcapsule and mechanical engineering application

One of the newest methods in the world to deliver drugs to target tissues is the use of chitosan and nano chitosan as biological nanocarriers. Other properties of chitosan include biocompatibility, antibacterial, antiviral, non-toxic, non-allergenic and film-forming ability. Another important application of polymers is core-shell in which two-bio layer natural polymer attached to each other for many mechanical and composite rebuild [25-31]. Injecting drug delivery, especially intravenous injection, is an easy way to achieve blood circulation by rapidly absorbing and transporting the drug to the site of action. However, this feature is usually accompanied by a rapid decrease in the level of the drug in the general circulation. In order for treatment to be more effective, it is best to maintain the drug level in its effective concentration range during the treatment period. Therefore, the systems have been tried to provide controlled drug release in the injection method. The drug carrier matrix in these systems must be biocompatible and biodegradable. It is also necessary for the system to have the ability to control the release of the drug for a long time in the general circulation, easy construction and orientation of drug carriers with active or inactive targeting mechanism to the desired location in the body.

Fig. 4 indicates the Assembly to function of microcapsule like chitosan microcapsule which are often powdery, very light and have a particle size between 1-1000 μm. Chitosan microparticle based systems have a wide range of applications in biomedical and pharmaceutical engineering. These microparticles usually have a porous structure and the drug trapped in them is released by the penetration mechanism. Therefore, the rate of swelling plays an important role in drug release. To date, chitosan microparticles have been used to transport various active agents, such as drugs, proteins, and antigens. Therefore, chitosan can be a good choice for these network carriers. The use of chitosan microparticles in drug delivery, with the help of their classification based on widely used preparation methods, has been expressed in the form of research that has been done so far. In general, chitosan is an abundant biopolymer that has many applications in medical engineering, especially in modern medicine, due to its properties such as biocompatibility, biodegradability, positive surface charge, and the ability to form fibers, nanoparticles, microparticles, and hydrogels.

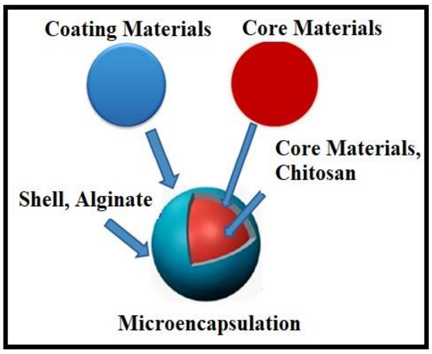

Fig. 3 The shell and core performance using natural polymers for drug release approaches

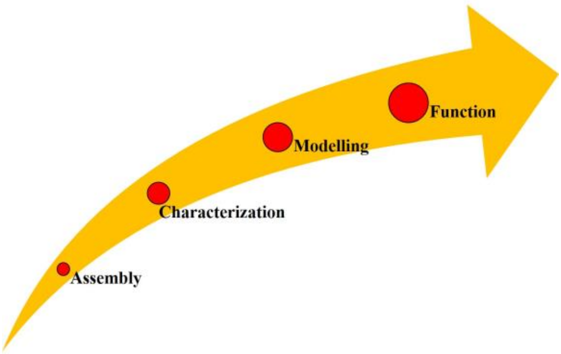

Fig. 4 Microcapsule mechanics: From stability to function and Assembly to function

Among these, chitosan microparticles, with the ability to prepare easily and quickly and a variety of preparation methods and compatible with a variety of active agents have been used many times as carriers of a variety of drugs and large molecules such as DNA and proteins. Several studies have shown that chitosan microparticles, in addition to targeted transfer of active agents, have other benefits such as crossing certain barriers in the body and controlled and delayed release as shown in Fig. 3 [32-45]. These advantages prove the high capacity of these microparticles in the field of drug delivery, so much so that despite the research age in the field of drug delivery based on chitosan microparticles, with the use of new and combined methods to prepare or modify them, we can continue to see the continuation of research in this field. According to statistics, after heart disease, cancer is the leading cause of death in the world. The disease is caused by the uncontrolled growth of cells and can lead to death when it progresses and spreads in the patient's body. Research shows that in cases where hyperthermia has been used in combination with radiation therapy or chemotherapy, or both, without a significant increase in side effects, the tumor response to treatment, local tumor control, pain relief effects, and patient survival can be increased [46-55]. Today, in the treatment of tumors of the breast, melanoma, glioblastoma, cervix, cervix, bladder, and rectum, the addition of hyperthermia to the usual treatment regimens is recommended. The treatment for hyperthermia is based on the destruction of cancer cells by raising the body temperature. In hyperthermia, it is possible to use different types of energy as a source of heat production, which include microwave, laser, ultrasound, and magnetic field. In hyperthermia, due to the uneven distribution of heat and thermometric limitations, it is not possible to prevent the rise in temperature in healthy tissues around the tumor. In other words, treatment of hyperthermia can effectively generate heat in tumors. But healthy tissues can also absorb microwave, laser, and ultrasound energy, which leads to adverse effects and damage to healthy tissues [56-60]. Magnetic nanoparticle hyperthermia uses a magnetic field to generate heat, which generates heat mainly through the effect of magnetic residuals [15, 18, 53]. Due to their adjustable physical and chemical properties, magnetic nanoparticles have shown a wide range of applications from medical diagnosis to treatment [61-65]. By combining a high saturation magnet with a suitable functional level, magnetic nanoparticles have advanced functionality that allows them to selectively attach to the desired cells or tissues and play a therapeutic role in them. In particular, iron oxide nanoparticles are being actively investigated to achieve highly efficient degradation of cancer cells through the treatment of magnetic hyperthermia [62-70].

In this context, nanotechnology offers a new and fundamental solution to magnetic hyperthermia, which is based on the use of magnetic nanoparticles to remotely generate local heat when applying a radio frequency magnetic field that raises the temperature in tissues and organs. The temperature in the tumor tissue rises to more than 43°C, which causes the necrosis of the cancer cells, but does not damage the surrounding normal tissue [65-70]. Among the available magnetic nanoparticles, magnetite has been extensively studied.

In recent years, significant advances in magnetite-nanoparticle hyperthermia have been observed. Both functional magnetite nanoparticles and alternating magnetic field generators have been developed. These results suggest that hyperthermia can not only kill localized tumors that are exposed to heat but also kill tumors in more distant locations, including metastatic cancer cells. In general, there are two types of strategies for targeting cells by nanoparticles, which include active and inactive strategies. Passive targeting can be done according to the characteristics and properties of various tumors by considering the environmental conditions of tumor cells, ambient pH, enzymatic activity, temperature changes, or by direct delivery of the drug to the cancer site

4- Application of nanoparticle diagnosis and treatment of cancer

In this study, an attempt has been made to briefly refer to the types of cancers, and the methods of coping and treatment based on magnetic nanoparticles that have recently been published in articles.

4-1 Lung cancer

Lung cancer is a disease characterized by uncontrolled growth in lung tissue. Most cancers that start in the lungs called primary lung cancers are carcinomas that arise from the epithelium. Common treatments for this type of cancer are radiation therapy, chemotherapy, and surgery.

4-2 Breast Cancer

Breast cancer is a type of cancer that disrupts the function of cell division in the breast. There are different types of breast cancer, and the type depends on which type of breast tissue cells are affected. Most breast cancers start in the lobules, and cancer cells can travel through the blood vessels and lymphatics to the outside of the back and spread to the rest of the body.

4-3 Ocular tumors

One ocular complication is melanoma ocular black tumor, which can be treated with high-load particle teletherapy.

4-4 Colon Cancer

Many colorectal cancers are caused by lifestyle factors and aging, and a small number are due to inherited genetic disorders. The reason for using these nanoparticles to fight this type of cancer is that among the various metal-based nanoparticles, silver nanoparticles (Ag-NPs) due to their antimicrobial properties and anticancer activity against various types of cancer, including breast, ovarian, brain, cervix have shown high biomedical relevance [62-75].

4-5 Prostate Cancer

Polylactic glycolic acid or PLGA as one of the most widely used drug nanocarriers, has desirable properties such as continuous drug release, biocompatibility, non-toxicity, non-immunogenicity, and biodegradability, the decision to synthesize these nanoparticles to counteract tissue.

5- Conclusion

Due to the spread of cancer and its epidemic and the importance of timely diagnosis and treatment and the amazing applications of nanoparticles, the need to pay for time and money in nanotechnology as an effective technology in combating this disease is determined. Therefore, in the last decade, following research and obtaining more information about tumors and types of cancer, a new method called nanotechnology has been proposed for the treatment of cancers. Nanotechnology is one of the most effective and less risky solutions with more benefits than chemotherapy and radiotherapy for patients, which is one of the new cancer treatments.

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