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A COMPREHENSIVE REVIEW OF MICROSPHERES AND ITS USES IN CANCER TREATMENT

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ABSTRACT

Microspheres are small free-flowing particles with 1-1000um diameter and can be used to overcome the problems of conventional drug delivery. By altering the materials, methods, and polymers the therapeutic efficacy of microspheres containing drug content can be altered. We have discussed about microspheres, their various types, techniques used to manufacture microspheres, also about the advantages and disadvantages of microspheres, how microspheres are used in the treatment of different types of cancers. Cancer microsphere technology is the latest form of cancer treatment. Cancer is a disease in which cells are abnormal they are the same as normal cells, with just a minute change in genetics or function. The main disadvantage of anti-cancer drugs is their lack of selectivity, which causes serious side effects and leads to reduction in effectiveness of treatment. As it is very difficult to treat abnormal cells in the normal way of conventional drug delivery system. Microsphere technology is perhaps the only method that can be used for site-specific action, without causing adverse effects on normal cells. Various microspheres that are designed or programmed to take advantage of microsphere technology in targeted drug delivery for treatment for various cancers. We have looked at the help of microspheres as a cancer treatment tool.

KEYWORDS: Microspheres, cancer therapy, types of microspheres, methods to prepare microspheres.

INTRODUCTION

Microsphere can be defined as very small spherical particles, which have a diameter from 1 to 1000µm (Lengyel et al., 2019; Saralidze et al., 2010). They are free-flowing particles and a microsphere consists of proteins or a synthetic biodegradable polymer (Saralidze et al., 2010). Conventional drug delivery had a plethora of shortfalls and disadvantages like dose frequency issue, toxicity, pH-problems, problem with dissolution, solubility, therapeutic efficacy, large amount of time required for drug development, adverse drug reactions and interactions, patient compliance problems, and many more can be added to this list (Tiwari & Pathak, 2011). To overcome these issues targeted drug delivery was developed for delivering the drug at a specific site, with a specific rate, which also reduces the toxicity to the neighboring organs/tissues (Hussain et al., 2017; N.G. Kotla et al., 2016; S. Singh et al., 2015, 2016). These advantages lead to a whole new era of drug delivery development which is marking new milestone every day from drugs for cancer treatment to meningitis, etc. Microspheres are also called smart drug delivery, in which the drug is coupled with the carrier (Niranjan G. Kotla et al., 2016; Sima Singh et al., 2015, 2018; Sima Singh & Lal, 2016). Specifically, the actively pursued goals in the anticancer chemotherapy method are the targeted drug delivery of anticancer drugs. Because the systematic anticancer drugs have a prodigious disadvantage of lack of selectivity for tumor tissues, that cause perilous side effects and results in a decrease in the efficiency of the treatment (Aldawsari & Singh, 2020; Sima Singh et al., 2020). This can be considered to be the major reason why microspheres are used along with the benefits like a microsphere can protect an unstable drug in both the situations before the administration and after the administration, also it reduces toxicity as it reduces the concentration of drug at site other than the tissue or the target organ, it reduces the dose frequency and the dose-volume, it can also make poorly soluble drugs more soluble, as in this there is particle size reduction which will enhance the solubility, microsphere provide a continuous and long therapeutic effect (Orowitz et al., 2020).

In our review paper, we found that there are many speculations about the original meaning/best meaning of a microsphere but there are majorly two types of the microsphere, one which has a microcapsule-entrapped substance distinctly surrounded by a distinct capsule wall and second in which micromatricess-entrapped substance is dispersed throughout the matrix.

Advantages of Microspheres (Darafsheh et al., 2014; Hossain et al., 2015)

1. Microspheres protect against unstable drugs both before and after the administration.
2. Other than tissues or target organs they reduced the concentration of drug at the site.
3. Dose toxicity is decreased by microspheres.
4. Microspheres enhance the solubility of poorly soluble drugs by particle size reduction.
5. Microspheres provide a constant and prolonged therapeutic effect.

Types of Microspheres

In our research of various review papers and research articles with the keywords 'types of microspheres,' we concluded that there are mainly 5 types of microspheres.

1. Bio- Adhesive microspheres
2. Magnetic Microspheres
3. Floating Microspheres
4. Radioactive Microspheres
5. Polymeric Microspheres

Bio-adhesive microspheres- The adhesion of a drug to the membrane through adhesive material can be defined adhesion of soluble polymers to water. These types of microspheres indicate the longevity of the application area. Adherence of drug delivery device to mucosal membranes such as buccal, ocular, rectal, nasal, etc (Hire & Derle, 2014).

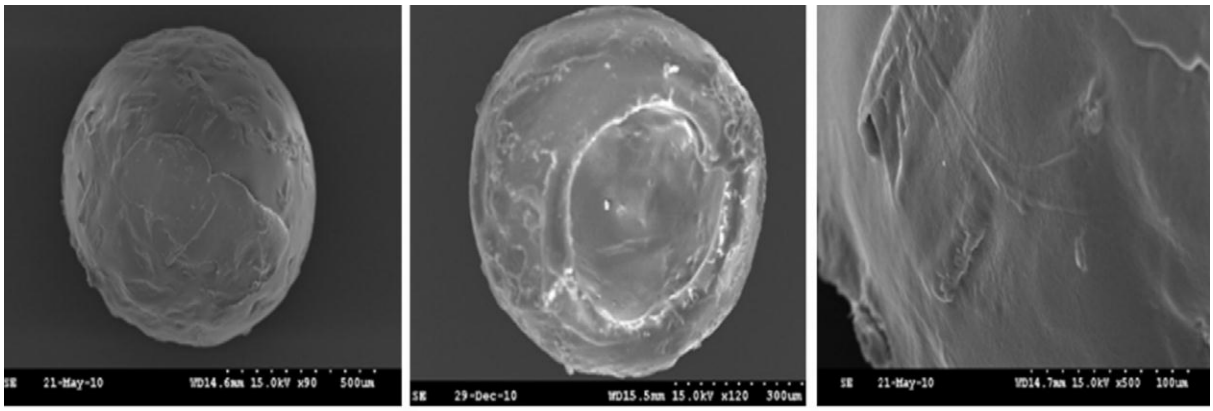

Figure 1: ***Scanning electron microphotographs of the hollow bio-adhesive microspheres showing (A) general appearance;(B) hollow structure;(C) surface morphology*** **(Y. Liu et al., 2011).**

Magnetic Microspheres - This type of delivery system is very important because it localizes the drug to the disease site. Which involves bigger amount of free-circulating drug replaced

by a small amount of (magnetically) targeted magnet. A magnetic response is received from magnetic field to magnetic carriers for incorporated materials that are used for magnetic microspheres which are chitosan and dextran (Luo & Li, 2019).

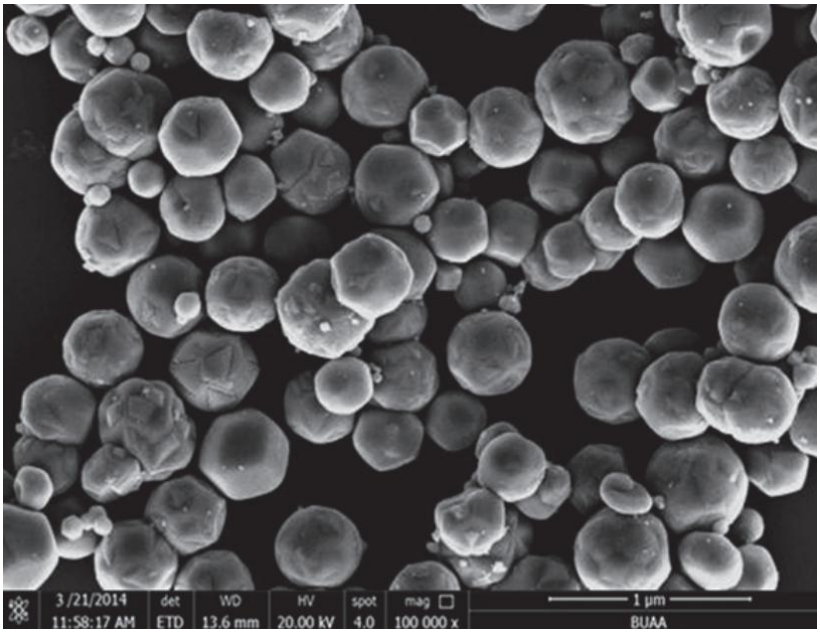

Figure 2. Scanning electron microscope image of PLA/Fe_3O_4 magnetic microspheres (Xiang et al., 2017).

Floating Microspheres- In floating microspheres the bulk density is less than gastric fluid, therefore, remains are buoyant in the stomach without affecting the gastric emptying rate. The drug is released slowly at the desired rate of site it also reduces the chances of striking and dose dumping (Mukund et al., 2012).

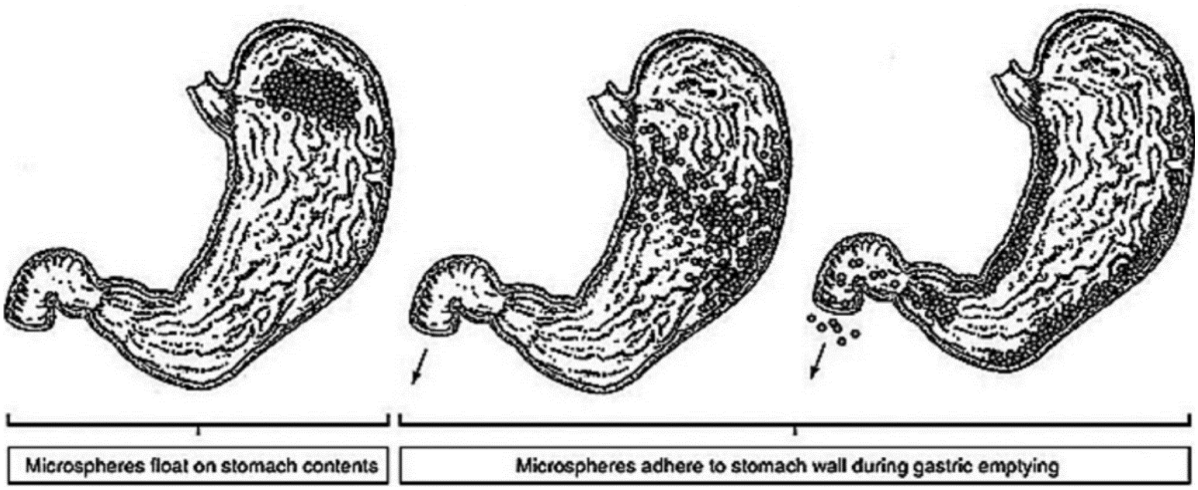

Figure 3: Mechanism of gastroprotection of floating microspheres having mucoadhesive polymer (Lei et al., 2005).

Radioactive microspheres – Radioactive microspheres for radio-immobilization therapy has size of 10-30 nm which is larger than the capillaries due to which they are tapped when they come across in first capillary bed. They are targeted to the tumor of interest by injecting into arteries. Radioactive Microspheres are capable of delivering high radiation doses to targeted areas without causing any harm or without damaging the normal tissues. α emitters, β emitters, γ emitters are the types of radioactive microspheres (Arranja et al., 2018).

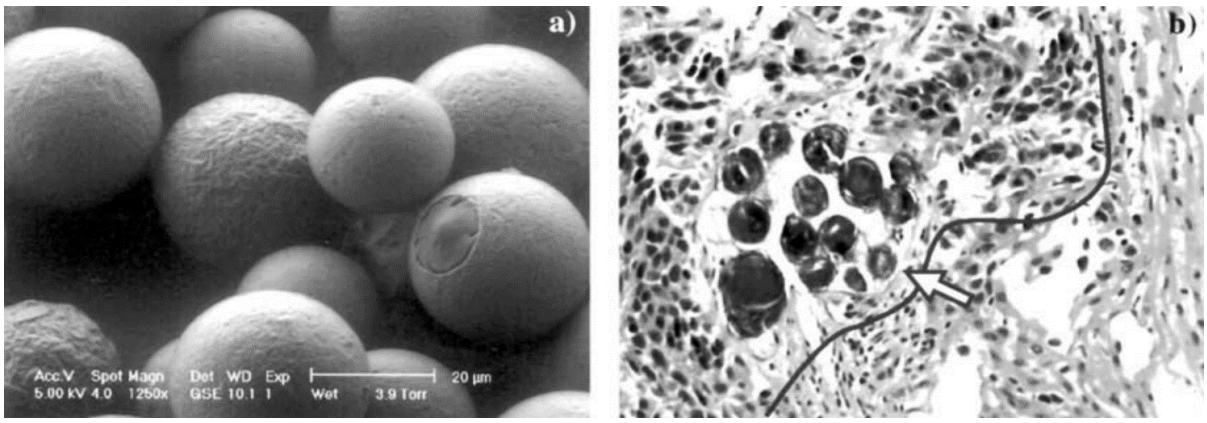

Figure 4: Scanning electron micrograph of holmium-loaded PLLA microspheres (a) white arrow depicts artery of tumour tissue in rat liver with radioactive holmium loaded microspheres. Artificial black line shows the border between tumour tissue (left) and liver tissue (right) (b) (Nijsen et al., 2012).

Polymeric Microspheres-The polymeric microspheres contain different types of polymeric microspheres like

1. Biodegradable polymeric microspheres
2. Synthetic Polymeric Microspheres

Biodegradable polymeric microspheres

Starch is a natural biodegradable, biocompatible and bio-adhesive polymer. The residence time with mucous membrane can be increased by these types of polymers, because they have high level swelling properties with aqueous medium (Jiang et al., 2015; Lin et al., 2015).

Synthetic Polymeric Microspheres

Synthetic polymeric microspheres are widely used in the clinical application, which is also used as bulk-forming agents, filling, embolic particles, and also as vehicles delivering drugs, etc. but there are some disadvantages of these type of microspheres like they often migrate away from the injection site and so may lead to potential risk, embolism and may also cause

further organ damage. Even though they have these disadvantages synthetic polymeric microspheres are safe and biocompatible (R, 2015; Saralidze et al., 2010).

Applications of Microspheres

Microspheres have a very large variety of applications and can be called very versatile –

Microspheres in chemotherapy – the most promising use of microspheres may be that they can be used as carriers for anti-tumor agents. Improved endocytic activity and leaky vasculature administrated microspheres. Soluble polyoxymethylene is used in the preparation of stealth microspheres. The accumulation of non-stealth microspheres in the Reticulo-Endothelial System (RES) can also be used for cancer treatment (Morimoto et al., 1981; Sugibayashi et al., 1977).

Microspheres for DNA Delivery- microspheres were recently used as a delivery vehicle for the plasmid DNA leading to improve plasmid DNA transfer and their stability in the bio-environment (Constantin et al., 2003; C. Qi et al., 2012).

Table 1: List of applications of microspheres.

SNo.	Applications	Material	Purpose
1	Cancer Therapy	Poly (alkyl cyano acrylate) microspheres with anticancer agents	Targeting reduced toxicity, enhanced uptake in-vitro and in-vivo stability.
2	Vaccine adjuvant	Poly(methyl methacrylate) microspheres with vaccines	It enhances immune response alternate acceptable adjuvant.
3	Ocular delivery	Poly (alkyl cyano acrylate) microspheres with steroids, anti-inflammatory a gents	Improved retention of drug/reduced wash out.
4	DNA Delivery	DNA-gelatin microspheres DNA-chitosan microspheres	It enhances delivery & significant higher expression levels.

Fluorescent microspheres- these are made of polystyrene or polyvinyl toluene, a mono distribution system ranging in size from 20nm to 4µm. For fluorescent dyes to enter microsphere pores swelling of polymeric microspheres is done by fluorescent microspheres. For physical entrapment of fluorescent dyes in the pores polymeric microspheres get unswelled (Feng et al., 2020; Gardner et al., 2018).

Use in Ocular Drug Delivery – many applications for drug-loaded ophthalmic delivery systems have been made in treatment of glaucoma, especially cholinergic agonists such as pilocarpine16. Short eliminating the half-life of aqueous eye drops can be extended from a

very short time (1-3 min) to a long time (15-20 min) using microspheres containing decaying materials such as poly alkyl cyanoacrylate (Wenguang Liu et al., 2008; Wenqiang Liu et al., 2019).

Adjuvant effect for vaccines – the beneficial effect of microspheres/nanoparticles with a solid or surface matrix vaccine has been shown in several studies in objects or oral treatment. "Kreuter & Co-workers" saw that the polymethyl methacrylate microspheres containing the antigen of the flu, making an important antibody response. Oral delivery of antigens with microspheres would be a good way to produce an increase in Immunoglobin A (Ig A) antibody response (Hanes et al., 1997; Qiu et al., 2014).

- Poly (lactide-co-glycolide) microspheres for lymphatic diagnostic agents.

Vaccine Delivery – the need for a vaccine is to protect against microorganisms and their toxic product. The right vaccine should meet the requirements of efficiency, safety, and convenience in use and cost. In 2000 limin et al. prepared a poly-microparticle using a solvent evaporation method as a drug carrier for insulin. Biodegradable delivery systems for vaccines given by the parenteral route can overcome the disadvantages of conventional vaccines (Desai & Schwendeman, 2013).

Imaging – imaging of a particular site depends crucially on particles size. Particles get entrapped in the capillary bed of the lungs when they are injected intravenously only those are spared which are administered through portal vein. For the scintigraphy imaging of the tumor masses in lungs this phenomenon is exploited in this there is use of microspheres labelled with human serum albumin. In gerbil's chitosan microsphere their oral administration. Gamma counter can be used to measure the radioactivity in tissues (Darafsheh et al., 2015; Hoang et al., 2015).

Gastro retentive controlled delivery system- When Floating systems are low-density systems, they float above the contents of the stomach (gastric contents) and stay in the stomach is longer than conventional dosage forms. While the system is floating above the gastric contents, the drug is released at the desired rates, which leads to an increase in the gastro-retention time as well reduces the plasma concentration fluctuations (Adibkia et al., 2013; Hajare & Rachh, 2020).

Implantable devices- Medically microencapsulation has also been used for the encapsulation of live cells and vaccines. Biocompatibility can be enhanced by encapsulation of artificial cells and biomolecules such as peptides, proteins, and hormones, which can block unwanted immune reactions that can lead to rejection. Isolation of materials is done with the help of microspheres until their activity is needed. The biotechnology industry uses microspheres to contain/store micro-organisms and their recombinant products to help in isolation these products (Ta et al., 2017; Tipnis et al., 2019).

Pharmaceutical applications- many microencapsulated pharmaceutical products are currently in the market, such as aspirin, theophylline, its products, vitamins, pancrelipase, antihypertensives, potassium chloride, progesterone and a combination of hormonal contraceptives (Ghosh Dastidar et al., 2018; Tarun & Jyoti, 2017). Microencapsulated potassium chloride (Micro-K, RH Robins, Richmond, VA) is used to prevent stomach problems associated with potassium chloride. The dispersibility of microcapsules and controlled release of ions reduces the chances of having a high salt concentration locally, which can lead to ulcers or bleeding. Microspheres have also gained strength in applications such as injection or inhalation products. The number of products available commercially does not indicates the amount of research conducted in this area or the benefits that can be gained by using this technology. Economic considerations have been an important factor in determining the number of drug products that are microencapsulated. Microencapsulation procedures are mostly very expensive and require a lot of money for setting up of equipment. The exception is the pan or spray coating and spray drying, for the necessary equipment it may already be available within the company. As most of the microencapsulation processes are patent protected it also adds up an additional cost (Wang et al., 2020).

Methods to prepare microspheres

There are many different methods to prepare the microspheres and the nature of the polymer, nature of the drug and the duration of therapy decide the techniques of preparation (Cheng et al., 2009; Zhang et al., 2012). There are some important Physical and Chemical factors that need to be controlled/monitored or taken care of during the manufacture of microspheres like-

1. Dispersibility and controlled particle size in aqueous vehicles for injection.
2. Reproducibility
3. The total mass of drug and polymer

4. No stability problem
5. Polymer to drug ratio
6. The molecular weight of the polymer
7. Particle size Requirement
8. The final product should be non-toxic
9. Release of the active ingredient with good control over a wide time scale.

Techniques use to prepare microspheres

In our review of various review articles and research papers on PubMed, science direct, etc. with the keywords (methods of preparation of microspheres), it has been concluded that there are mainly 8 methods to form microspheres.

1. **Size Emulsion Techniques** (Zhao et al., 2017)
2. **Double Emulsion Techniques** (Bahadoran et al., 2020)
3. **Polymerization** (Zhai et al., 2009)
4. **Phase separation coacervation technique** (N.R, 2015)
5. **Spray drying** (Zhou et al., 2019)
6. **Solvent Extraction** (Belali & Chaerunisaa, 2019)
7. **Solution-enhancement dispersion method** (Novoselov et al., 2004; Yu et al., 2009)
8. **Wax coating hot-melt method** (Mathiowitz et al., 1990)

Single emulsion technique

There are several proteins and carbohydrates, prepared by this method. Where natural polymers are dissolved in an aqueous medium and then dispersion in the oil phase is done therefore non-aqueous medium. That is the first step and the next step consists cross-linking is done in two ways.

- **Cross-linking with heat**: in this a dispersion is added into the hot oil. Thermolabile drugs are not sported by this method.
- **Chemical Cross-Linking agents**: through agents i.e. formaldehyde, dichloride acid, glutaraldehyde, etc. but there is a problem with over-exposure active ingredient in chemicals, when added at the time of preparation and exposed to centrifugation, washing, and separation. Water in oil (W/O) emulsion is formed when chitosan solution (in acetic acid) is added to liquid paraffin that also contains a surfactant. Metformin hydrochloride microsphere prepared by using a 25% glutaraldehyde solution as a cross-linking agent.

Double Emulsion Technique

The composition of many emulsions i.e water in oil in water (W / O / W) is prepared by pouring the primary water in oil (w / o) emulsion into polyvinyl alcohol aqueous solution. This water in oil in water (w / o / w) the emulsion has a stirring t constant of 30 minutes. In a time span of 30 minutes add small amount of water slowly. Use a vacuum to dry the microcapsules that are collected by filtration. This method is better for water-soluble drugs, peptides, proteins, and vaccines. Synthetic polymers as well as natural polymers can be used for this method. In a lipophilic organic continuous phase the aqueous protein solution is dispersed. This protein solution may contain active ingredients. Disseminate in the oil/organic phase homogenization/vigorous i.e. formation of the first emulsion then add to the water solution of poly vinyl alcohol (PVA) which means that more emulsions are now formulated in addition to aqueous phase denaturation / Harding after this separation, washing followed by drying and collection of genistein chitosan microsphere were prepared by oil in water in oil (o / w / o) multi emulsion technique by (Wu and Li,2002).

Polymerization Techniques

There are 2 techniques used to prepare the microspheres in this category –

Normal Polymerization

In Bulk polymerization, a monomer or a mixture of the number of monomers is usually heated with an initiator or the catalyst to initiate polymerization. The polymer so attained can be shaped like microspheres. Drug loading can be done through medicating during the process of polymerization. It is a method of pure polymer formation but it is very difficult to eliminate the heat of the response affecting ingredients of active thermolabile ingredients. Polymerization of suspension is performed at lower temperature and is referred to as pearl polymerization in which monomer mixture is heated with an active ingredient such as dispersion of droplets in a continuous aqueous phase. Microsphere with size less than 100um are obtained by suspension technique.

Interfacial Polymerization

Disperse phase is enveloped by a polymer film which is formed by reaction of various monomers by reaction between two immiscible liquid phases. In this process the two monomers react; one dissolved in the continuous phases while the other is dispersed in aqueous natured continuous phase in which emulsification of second monomer takes place.

Spray drying and spray congealing

The concept of how to stop spraying depends on solvent removal or cooling solution for both to stop spraying & spray mixing. In spray drying evaporation is the basic principle whereas phase inversion from liquid to solid is the basis of spray congealing. Both processes are the same, except for energy flow. Therefor an ideal process is spray drying in which the end product must comply accurate standard of quality related to residual moisture content, bulk density, shape of particle and size distribution of particles.

Wax Coated and Hot Melt

In this slow cooling is done after the polymer is dispersed in suitable dispersion medium to form microspheres. Microspheres can be easily fabricated for polymers having low melting point. Wax is used mainly for the coating and coring. Molted wax is used for encapsulation of drug by dispersion in it. Wax suspension disperses at the top the speed into the cold solution for example liquid paraffin. Stir/agitate the mixture for one hour. The suspended microspheres are collected from the solvent after the external phase is decanted. Let it dry in the air. It's not expensive the method when comparison is done with other methods and in this the release of drug is very rapid. Desired characteristics can be achieved by mixing the coating materials in in order and for this carnauba wax, bee wax are mainly used.

Solvent Evaporation Method

This method is preferred for the formation between polymer solution and immiscible continuous phase in aqueous oil in water as well as non-aqueous water in oil of the emulsion. Bogataj et al. (2000) used evaporation method on liquid paraffin and acetone solvents to prepare microspheres. The mixture of drug solution and in acetone formed by dispersing it in chitosan solution was stirring in liquid paraffin for emulsification process.The microspheres suspension was filtered and the its drying is done leading to its washing. Agglomeration needs to be prevented by adding a agglomeration preventing agent and for that magnesium stearate is used as one. From results of the study it was concluded that increasing the amount of magnesium stearate used microsphere preparation decreases the average particle size.

Coacervation Technique- Two immiscible liquid phases are used are obtained from simple separation of micromolecular solution in this technique. A solution is formed from the solubilized polymer. Reservoir type system is formed by this method, for which encapsulated water soluble drugs are example(peptides, proteins, etc..). Formation of coacervates also called polymer rich phase is affected by decreasing the solubility of polymer in organic phase

and this is the principle used in it. The first polymer is phase separated and the drug particles are engulfed when the dispersion of drug particles in a solution polymer is done and an incompatible polymer is added to it. For hydrophilic drugs like steroids the matrix type preparations can also be produced. The solidification of polymer is done when non-solvent is added. Butadiene is used an incompatible polymer to prepare poly lactic acid (PLA) microspheres. For solvents that are toxic in nature like organic solvents and glutaraldehyde this method is not suitable. Berthold et al.(1996) used precipitant in the form of sodium sulphate to form chitosan microspheres loaded with prednisolone sodium phosphate. Decrease in solubility of chitosan by addition of sodium sulphate leads to precipitation of chitosan as a poorly soluble derivative.

Solvent Extraction

The method of solvent extraction involves the preparation of micro particles by extraction of organic solvent which involves the removal of organic phase. Isopropanol can be used as an organic miscible organic solvent. By water extraction, the Organic phase is the same has been deleted. The duration of microsphere hardening can be reduced in this way. Solvent removal rate by extraction method depends on water temperature, average emulsion volume in water, and melting profile polymer.

Application of Microspheres in Cancer Therapy

In a broad sense, there are mainly 277 different types of cancer disease. Scientists have identified a different stage of cancer, indicating that several mutations of genes are involved in cancer pathogenesis(Yeung et al., 2015). These genetic mutations lead to abnormal cell proliferation. Inheritance disorders caused due to hereditary factors play an important role in increasing cell growth. Technological advances in biopharmaceutics and molecular techniques help by providing additional information which is helpful in early detection and so proper treatment could be provided to the patient. Drug effects in patients and cancer can predict and treat some aspects of side effects. In recent years, carcinogenesis mechanisms have been discovered by molecular genetic studies. The results of these studies have led to an improved understanding of the role of inherited disorders in cancer formation.

Targeted delivery of anti-cancer drugs is one of the many deliberately pursued goals in anticancer chemotherapy (Rajput & Agrawal, 2010). The worst of the systemic anticancer drugs is their lack of selection of tumor tissue, resulting in stiffness and side effects at lower levels of treatment. Any strategy when the cytotoxic drug is targeted at a tumor, therefore

increasing the therapeutic index of the drug. How to improve cancer treatment and reduce systematic toxicity. Modern medicine is effective to achieve disease-free survival for large number of cancer patients. In most cases, however, medical intervention is effective only in increasing the life of the patient from a few months to a few years. Cancer is a multi-faceted disease in which we have to avoid the destruction caused by it (Pradhan et al., 2017). Therefore, multimodal treatment is required, with or without surgery targeted delivery of anti-cancer drugs is one of the many deliberately pursued goals in anticancer chemotherapy(Willmott & Daly, 2020). Modern medicine is effective to achieve disease-free survival with a good amount of cancer patients. In most cases, however, it is medical intervention is effective only in increasing the life of the patient from a few months to a few years. Medications are always available found, and developed, by the identification of neoplasia, and given the most important. In all forms of treatment, a common thread is the need to identify to avoid the side effects of the drug. A few years ago, microspheres were shown to prefer vascular abdomen endothelial cells. Also, a handful of articles highlight the ability to identify these verses in plants in various parts of the body, with advanced use of microsphere delivery systems. The use of microspheres as a drug delivery system certain benefits, such as additional performance and reduced the toxicity of the implants to untreated cells and tissues(Pundir et al., 2012).

Disadvantages with conventional cancer treatments

Conventional chemotherapy refers to the treatment of certain diseases, especially cancer, by using chemical substances and types used over the past fifty years or more. Conventional chemotherapy is given one drug at a time or several drugs simultaneously or combined with other cancer treatments, such as radiation therapy, surgery followed by several chemical cycles. In general, chemotherapeutic drugs effectively damage rapidly growing cells and prevent mitosis by inhibiting DNA synthesis and blocking cellular machinery involved in the cell cycle process, which in turn causes apoptosis, a planned cell death. Alkylating agents are the oldest used chemical products since the late 1940s after it was discovered that the use of mustard gas in World War I caused leucopenia. It has been proven that various drugs can destroy tumor cells by creating normal apoptotic mechanisms but the mode of cell events required to activate the apoptosis process is different. Although chemotherapy is an important means of controlling cancer due to the difficulty in choosing the dosage, the deficiency that produces cytotoxicity in normal cells and, rapid drug metabolism, both internal and external drug resistance varies from patient status and especially side effects, chemotherapy success is

limited to date. Chemotherapy is based on its ability to kill fast-growing cells, a key component of cancer cells. However, chemotherapy kills and normal cells divide; e.g. bone marrow cells, intestines, etc. For this reason, the scope and effectiveness of chemotherapy are restricted. The growing strength of cancer cell's resistance to chemotherapy is one of the major obstacles to conventional chemotherapy. In drug-resistant cancer cells, exposure to small-dose pumps such as p- glycoprotein and intercellular antioxidant efflux prevents chemotherapeutic agents from entering cells. Many critical types of equipment are involved in drug treatment and chemotherapy. Genotoxic drugs used in chemotherapy can cause mutations in genes that cause increased DNA damage, leading to cell death. But in some cases, mutations in genetically modified proteins prevent the binding of drugs to a target protein, which can counteract the chemical effect. The potential for cancer cells to produce genetic mutations and genetic modification by genetically modifying proteins that reduce apoptosis plays a key role in producing drug resistance to chemotherapy. Mistake in the apoptotic pathway through genetic modification of normal cells including tumor genesis and may be resistant to chemotherapy with apoptosis chemotherapy. In a type of cancer when the drug delivers through the circulatory system, chemotherapy fails because of improper blood flow to the tumor cells. Patients with late-stage cancer may not be completely cured and face a high risk of premature death because they may not tolerate the side effects of chemotherapy. Therefore, side effects are one of the biggest and leading problems of chemotherapy and often reduce its use. Side effects occur most often when chemotherapy damages healthy cells that maintain body function and appearance. Different side effects occur depending on the type of drug. For example, alkalyting agents and anti-metabolites directly damage DNA to prevent cancer cells from producing; therefore, they can cause long-term damage to the bone marrow, which can eventually lead to severe leukemia. Hence it can be concluded that even though conventional cancer treatment can treat the patients suffering from life-threatening cancer but it also has many side effects and disadvantages due to which conventional cancer treatment could be quoted as “Necessary Evil” for the cancer patients.

Liver Cancer

Microspheres are used as a surgical bridge or transplantation or anti-radiation therapy for cancer. For patients diagnosed with colorectal carcinoma, mostly death is caused by hepatic metastases (Y. Qi & Liu, 2021). Cytoreductive therapies in cancer treatment can be categorized as the transcapsular used method or trans-vascular pathways. Thousands of treatments for that exploitation of the trans-arterial route are based on a foundation that

metastatic tissues receive blood supply trough arterial route, then site distribution occurs, in contrast to normal hepatocytes. Preferential delivery of material to the peritumoral vascular plexus is done by injection of hepatic artery. Microspheres of an appropriate diameter will lodge in the peritumoral vessels called embolization process when a suspension of particles injected via the hepatic artery. If appropriate tumor doses can be delivered selectively without damaging the adjacent normal tissue the radiation can be used to destroy tumor (Bester et al., 2011).

Breast Cancer

In the breast, microspheres loaded with cytotoxin are delivered through a catheter, which is inserted surgically directly either in the subclavian artery or in the branch subclavian artery, usually thyrocervical trunk (de Araújo et al., 2019). Selective perfusion, however, can be found with the angiographic placement of catheters directly in the internal mammary artery. When internally-arterially administered these microspheres are controlled by blood flow to the capillary bed where they attach and let go of their medical burden on the target organ. Breast cancer cells target delivers a single pulse of adriamycin-loaded albumin microspheres using radiologically induced interiors mammary tube vein. Animal studies have shown that adriamycin-loaded albumin microspheres by radiologically placing an internal mammary artery catheter. Radiation therapy should be considered for women at high risk of local regional tumor recurrence (women with advanced primary tumors, more or at least four lymph nodes) (Sima Singh et al., 2021).

CONCLUSION

Microsphere technology, though still in its infancy, has great potential for cancer treatment. It is a technology that will grow in the years to come on and maybe the human race will get 100% cure of cancer. Drugs can be targeted at specific sites in the body using microspheres. The can be achieved by targeting a drug somewhere in the body (for example in the lungs), in a group of cells (for example, kupffer cells) even in intracellular structures (such as lysosomes or cell nucleus). The rate of drug release is controlled by the drug molecules and polymer and various other factors like polymer resistance to corrosion, surface area and porosity of microspheres. Controlled drug release from microspheres occurs by the distribution of the drug through a polymeric excipient. It is a unique technology for the controlled release of topical agents and contains small beads loaded with an active agent and has use in oral and other biopharmaceutical drug deliveries as well.

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