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A STUDY ON MICROENCAPSULATED NANOPARTICLE & IT'S APPLICATION IN PHARMACEUTICAL INDUSTRY

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Abstract

With advancements in technology in the area of drug delivery systems, the new concept of encapsulation of the nanoparticles has been looked upon with promising eyes by the scientists. Oftentimes earlier the use of nanoparticles for the target delivery of the active compound failed because the vehicle or the carrier nano particle got either destroyed or structurally and molecularly disturbed making it unfit to carry the drug or the active compound. In order to protect the carrier molecules from the environmental stress or damage the idea of encapsulation was proposed. Encapsulation is a technique in which the nanoparticle is coated with a protective and inert substance so that it is not damaged structurally or chemically on the way to the delivery. Nanoparticles find use in many fields such as the pharmaceutical sector, cosmetic industry as well as in many researches related to the biomedical field. These fields can have a breakthrough technology of encapsulation which can enhance the performance of various products associated with these industries. In this paper the process of microencapsulation of the nanoparticles will be discussed in detail. The paper will also include the advantages and disadvantages of microencapsulation of the



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nanoparticles. This review paper will give an account of different methods of encapsulation. Lastly the areas and fields where the encapsulated nanoparticles can be used will also be discussed in detail.

[1] INTRODUCTION

In the present era the new discoveries in the field of very small particles has led to discovery of micro, nano, picometer size particles that are now widely utilized in various industries for example making novel drug delivery systems in pharmaceutical industry and ultra effective skin care products in cosmetic industry. The realm of research advancements in fields of nanotechnology as well as encapsulation techniques have enabled the scientists to develop micro and nano technology products that are way more stable, advanced and effective in terms of performance. Encapsulation can be defined as a method in which the active substance is enclosed with non-reactive material in order to protect the active ingredient and enable its controlled release at the target site. In the present time two types of encapsulations are primarily performed; one is micro encapsulation and other is nano encapsulation. Micro encapsulation is the technique in which various substances are coated within different materials on a micro scale. This process of encapsulating a nano sized material is called nanoencapsulation. Microencapsulation technique has been extensively utilized in numerous industries since many decades while nanoencapsulation is a fairly newer idea. Microencapsulation is a technology that has wide utility in pharmaceutical industries, agrochemical, food industries and cosmetic industry.

Nanoparticles are the materials that have the size range between 1 and 100 nm. These particles find utility in fields of biosensors, drug delivery and microarray tests and tissue engineering. Nanotechnology assigns curative agents at the nano scale level while developing nano medicines. Nano particles are small sized nano spheres because they consist of materials designed at the very basic level of atoms. Due to this small size and functioning at the molecular level these particles move freely in the human body as compared to bigger particles. These nanoscale sized particles showcase unique mechanical, magnetic, electrical, structural, chemical and biological properties. Nano medicines have become much popular and much appreciated in today's time. This is because of the major advantage of using the nanoparticles that help in encapsulating drugs and also sometimes help in attaching therapeutic drugs so that the drug delivery is efficient and is carried out in a controlled manner. Micro encapsulation refers to the process of encapsulating a nano particle in a coating of micro size and inert material to protect the active nanoparticle and enable its control release.

The use of Microencapsulated nanoparticles opens fresh avenues for drug delivery vehicles. Through research conducted by scholars it was demonstrated that by the use of micro



encapsulated nanotechnology, the treatment for diseases like glioblastoma, a devastating brain cancer, is possible. Several micro encapsulated nano particles which possess biodegradable polymers can ensure fulfillment of the stringent requirements that are needed for some particular type of drug delivery systems. Some of these include the capability to get transformed into an aerosol, biocompatibility, stability during the process of aerosolization, ability to target specific sites or cell populations, releasing the drug in a predetermined form and degrading within a certain period of time. Microencapsulated nanotechnology offers site-specific and target oriented drug delivery of a particular medicine and thereby proving as a boon for the treatment of chronic diseases. In recent times, this technique has been extensively used in the field of pharmacy to form various micro encapsulated nano medicines. For example - use of chemotherapeutic, biological and immunotherapeutic agents in the treatment of various diseases.

[2] TECHNIQUES OF MICROENCAPSULATION

1. Coacervation: Coacervation is one of the techniques for microencapsulation that allows the fabrication of nanoparticles. This process is a result of phase separation between the colloid rich and colloid poor layer. It is achieved by the use of a wall made up of polymers. This wall is used to layer the core material from the outside. This process of covering and coating is done by changing the physical as well as the chemical properties of the coating material through alteration in pH, ionic strength or temperature. A solution is prepared with the core material as well as the coating wall material which is immiscible in nature. Then, by altering the pH, temperature or ionic strength a liquid phase of this coating material is separated from the polymeric solution of the core material. This process leads to the formation of tiny liquid droplets called the coacervates which constitute a polymer-rich dense phase. The separated core material is gradually covered by these coacervates and ultimately result in the formation of the microcapsules. The functioning of this process is such that there occurs an electrostatic interaction between two liquid mediums which results in the transformation of liquid into gel. This is called ionic gelation and this further leads to the formation of coacervates. This method of microencapsulation is extensively used for the encapsulation of hydrophilic molecules in a solution. There can be two ways of using this technique: (i) Simple Coacervation and (ii) Complex Coacervation. A simple coacervation is the one in which the polymer used is single like ethyl cellulose or gelatin. For example - For the purpose of simple coacervation, the polymer sodium alginate is mixed in water along with an active compound which is generally oil. This active compound along with water forms oil-in-water emulsion and later the oil gets encapsulated in the separation process This emulsion is added into a gel-forming medium such as calcium chloride in the form of droplets. This interaction between the ions of sodium alginate and calcium chloride results in the formation of an insoluble polymer called calcium alginate. On the other hand, a complex coacervation is the one in which there is an application of more than one polymer. In this technique there is a process of neutralization of two oppositely charged polymers in aqueous solution. For example - Use of two polymers gelatin and alginate for the process of complex coacervation. The first polymer, gelatin, is used to obtain the positive charges by solubilizing it in water at the pH level which is acidic in nature. Then the second



polymer, alginate, is also solubilized in water at the pH which is basic, in order to get negative charges. Proper homogenization of microencapsulated active compounds is done by mixing it with alginate solution. After the mixture of active compounds with alginate the entire solution is thoroughly mixed with the phase that contains gelatin. Then temperature is increased upto the level that there occurs a chemical reaction between the compounds, gelatin and alginate. Hence, as a result of this chemical reaction, the active compound is encapsulated by the formation of polycationic-polyanionic polymer coating it completely and also which is insoluble in nature.

2. Cyclodextrin inclusion: Cyclodextrins are a type of polysaccharides which are a result of starch biodegradation. These cyclodextrins can form inclusion complexes with various organic compounds. These are used for the process of encapsulation as they can be a host to active molecules through their internal hydrophobic cavities. Cyclodextrins possess internal non-polar cavities and on the surface they possess hydroxyl groups. The hydrophobic interaction that takes place between the surface of cyclodextrin and the other compounds leads to the generation of inclusion complexes of cyclodextrins. Numerous methods can be used to obtain the inclusion complexes with cyclodextrin inclusion technique, such as: (i) Coprecipitation method, (ii) Freeze drying or lyophilization method and (iii) Spray drying method. (i) Coprecipitation method - It is suitable for the non-water-soluble substances. In this method, two compounds are used, one compound is to be encapsulated while the other is an organic solvents which can be a solvent like chloroform, diethyl ether or benzene etc are mixed together. On the other hand, a solution of cyclodextrin with water is prepared. This solution is added to the solution earlier prepared using the organic solvents and these are mixed well with heating. After the mixture cools down, the complex crystals can be obtained. Later the resultant of this technique are dried using an organic solvent. (ii) Freeze drying or lyophilization method - this technique is best suited for the compounds which are thermolabile in nature. A mixture of cyclodextrin and a compound to be encapsulated is thoroughly mixed in water by stirring it rigorously. This stirred solution is freeze dried. As it freezes, there is a formation of power of the mixture which can eventually be washed with an organic solvent and dried under vacuum. (iii) Spray drying method - This technique highly useful when there is a presence of thermostable molecules. Cyclodextrin and the other compound are mixed in deionized water. Then the mixture is dried with the help of a spray dryer. This is majorly used in the food industry as cyclodextrins can be used for encapsulating the flavor compounds. This is because the cyclodextrins can enable enhanced protection, retention and also ensure controlled release.

3. Emulsification: Emulsification technique is extensively used for the purpose of encapsulation. In this technique, the core material is dispersed in an organic solvent which contains the coating material. Then this dispersion is emulsified in the oil or water. Along with this an emulsion stabilizer is also added to the mixture. The process of encapsulation here is quite simple as the core to be encapsulated is covered by a layer formed by a compact polymer during the process of evaporation of the organic solvent from this mixture. This technique is widely used in the pharmaceutical industry because it has simplified processes that require less hassle and saves time. The encapsulation of enzymes and microorganisms can be done very easily through this technique.



4. Extrusion: Extrusion technique is widely used for the purpose of obtaining highly dense microcapsules. In this method the core material as well as the coating material is immiscible. In the process of encapsulation under this technique, the core and the coating materials are passed through concentric nozzles. This results in the formation of droplets which contain both the core as well as the coating material. For the purpose of solidification of these droplets the cooling process is undertaken. Another method for solidification is through gel bathing in which the droplets that are collected are complexed to solidify. This technique of encapsulation is different from other techniques as the encapsulates formed using this technique are larger than the ones formed using other techniques.

5. Fluidized Bed Coating: This technique of encapsulation uses the process of spraying coating material all over the fluidized core material. In this technique the core material is necessarily fluidized using air and only then the spraying of the coating material takes place. There are various types of fluidized bed coating methods, such as - (i) Bottom spray (ii) Top spray and (iii) Tangential spray. In fluidized bed coating, there are various factors that affect the coating efficiency of the coating material, such as -(a) coating material's feed rate, (b) nozzles' pressure for atomization, (c) velocity and (d) temperature of the air inside.

6. Spray Cooling: Spray cooling and spray drying methods of encapsulation are quite similar in their process. However, the difference between the two is that in the spray cooling method the air used is cold rather than hot. In the spray cooling method, the core material and the coating material are mixed and atomized to generate a moist fog inside a chamber. Inside this chamber the cold air keeps flowing. While the cold air keeps flowing, it builds an atmosphere of low temperature within the chamber. This reduced temperature leads to the solidification of the micro droplets and hence forms microencapsulated powder.

7. Spray Drying: Just like the spray cooling method, here in spray drying method as well, both coating and core materials are mixed and atomized to be formed into a moist fog inside a chamber. However, in this technique, the air that is used inside the chamber is hot unlike in the case of spray cooling where the air inside the chamber is cool. This hot air inside the chamber converts the mist into powdered form. In order to obtain varied sized particle powder, the alteration can be made in the characteristic of the feed solution and also the condition in which this operation takes place. This method traps the core material into the powdered form so that they are easily encapsulated. This method of encapsulation is extensively used in the pharmaceutical industry due to various advantages. Some of these advantages are: (i) it is suitable for different encapsulating agents, (ii) requires less cost, (iii) flexibility with the process, (iv) can be dynamically used with any material (v) scaling up the process becomes easy.

[3] ADVANTAGES OF USING MICROENCAPSULATED NANOPARTICLES

The use of microencapsulated nanoparticles has several advantages, some of which are discussed as follows:

- **Protection from physical and chemical degradation** – The physical or chemical stability of any drug if altered leads to deteriorated potency of that drug. The quality of that drug is



reduced and hence its effectiveness is negligible. The physical degradation takes place when there is change in the appearance of any drug like its color, brittleness, hardness, change in taste, settling, caking etc. The chemical degradation takes place when the chemical compounds of the drug break-down into simpler compounds. The ways in which this chemical degradation happens are – oxidation, isomerization, polymerization, hydrolysis and decarboxylation. Use of micro encapsulated nanoparticle drug delivery systems enables the protection of drugs from such degradations as the upper coat of micro particle is an inert material which is chemically unreactive hence enables chemical protection and physically this material is stable hence protects from physical degradation as well.

- **Sustained delivery** – When the delivery of a drug is carried out by those methods that support longer retention of the drug in the body to provide long term benefit, it is called sustained drug delivery. Through the use of micro encapsulated nano technologies this can be done very easily especially for those drugs that have fast metabolization rate or those drugs that are very quickly removed from the body after the intake.
- **Improved tissue macrophages distribution** - Macrophages are distributed in the tissues to fight against any pathogen or foreign agent. They are the most flexible that are helpful in treating the inflammatory respiratory diseases. The role of macrophages is to maintain the homeostatic tissue process, repair the tissues and improve immunity. The micro encapsulated nano drug delivery system enables better distribution of these macrophages in the tissues hence enabling stronger immune responses.
- **Enhancement of stability** – Drug stability is assessed by the retention of drug substance from the time it is manufactured to the time of its storage throughout its shelf-life. It is necessary that the drugs remain stable throughout its useful life so that its ability to treat a particular disease is not degraded. With the use of a micro encapsulated nano drug delivery system this stability is efficiently achieved. The drugs remain in their best form from the time they are manufactured to the time they are used in future.
- **Enhancement of pharmacological activity** - The use of novel drug delivery systems like micro encapsulated nanoparticles, which have very small size, the pharmacological activity of the drug is enhanced manifold. due to the small size the pharmacological activity also enhances because collectively their surface area increases which leads to more drug absorption. Hence it allows better drug absorption and an effective drug delivery at the targeted site.
- **Toxicity Prevention** - The advanced nanoparticle drug delivery systems acts as a protectant for the tissues and cells of the body against any toxicity produced by residual components of a drug. The benefit of using micro encapsulated nanoparticles is that it allows the drug to reach the site of action as and when required by the body. These delivery systems are chemically stable and ensure safe chemical composition is maintained within the body.
- **Increased bioavailability** - The bioavailability of a drug is defined in a way that it is a portion or component of the drug that enters the blood circulation system of the body and is able to show its active effects in the body. A drug is considered potent and highly effective if it has higher bioavailability. To enhance the bioavailability of any drug, the carriers like micro encapsulated nanoparticles are used that are a part of novel drug delivery systems and



effectively enhance the bioavailability of the active compound.

[4] APPLICATION OF MICROENCAPSULATED NANOPARTICLES

1. Pharmaceutical Sector: In the pharmaceutical sector mainly the micro encapsulated nanoparticles are used in drug delivery systems. By definition a drug delivery system is an advanced technology of formulation of various carrier compounds that enable targeted delivery and controlled release of active ingredients of the drug. The use of micro encapsulated nanoparticles in drug delivery enables the delivery of the active pharmaceutical ingredient of the drug to reach the target site selectively without affecting the non-target cells, organs or tissues. The microencapsulated carriers enable the controlled release of the drug overtime and produce more prolonged and efficient results. In order to improve the efficiency and quality of prevailing pharmaceutical materials and enhance their performance micro encapsulated nano nanoparticles can be successfully used. Another use of microencapsulation is to mask the bitter taste of a drug by coating it with some sweetener. This will not only provide good taste but since the coated material would be inert it will provide protection and stability to the active drug. Microencapsulation finds another use in enhancing the solubility of an otherwise insoluble drug.

2. Food & Agriculture Industries: There is wide use of microencapsulated nanoparticles in the food and agriculture industry. The use of micro encapsulated nano material is used as major ingredients to improve flavor, color, texture to enhance the shelf-life of the edible products. Moreover, the micro-encapsulated nanoparticle ingredients can also be used to infuse the edible product with compounds imparting functional health benefits, such as antioxidants and probiotics in basic foods without actually damaging the beneficial compounds. The major reason why microencapsulation is used in making of antioxidant and probiotic containing edibles is because it keeps these compounds stable and enhances their bioactivity and bioavailability. In the food industry generally the active compounds are encapsulated and put in the beverages which enables fast reach of the compound as the beverages are liquid. Another very common area of use of microencapsulated nano particles is bakery products. In bakery products this technique is used in making the food coloring that may have a beneficial compound within it. In baking industry encapsulation is done of the food dyes to protect them physically and chemically as they are subjected to excessive heat in the oven. Therefore in order to keep the color intact and taste better the encapsulation enables stability of the dye compound and its protection is also ensured.

3. Cosmetic Industries: The use of micro encapsulated nanoparticles in the cosmetic industry has many benefits such as it protects the active ingredients of the product while its usage both physically and chemically. Moreover, this technique allows slow and even distribution of the encapsulated active ingredients. This in turn helps in better absorption on the surface of the skin and enhances the drug penetration level. Microencapsulation helps in keeping the active nano ingredients completely unaffected until they are applied to the skin. Microencapsulated nanoparticle containing skin care products are effective in reducing wrinkles, minimizing dark spots and nourishing the epidermis. In the creams and skin care



products that contain active retinol nano particles that are encapsulated with micro size particles the microencapsulated pigments which are microencapsulated are released as they come in contact with the skin. This enables a healthy glow and improves the skin quality. Moreover, it releases the active retinol that attaches itself to the bottom of the skin surface and then gradually releases the anti-aging active ingredients. Similarly, oil and ceramides can be used for such purposes. In this combination of oil and ceramide, the ceramide is coated with a layer of oil through the process of emulsification. Hence, as the product is applied on the skin, the bubbles of oil plump the skin from within and microencapsulated ceramides illuminate the skin.

[5] THERAPEUTIC APPLICATIONS

- **Cancer Therapy:** Nanoparticles encapsulated with chemotherapeutic agents reduce damage to healthy tissues.
- **Gene Therapy:** Delivery of siRNA or DNA for correcting genetic disorders.
- **Vaccination:** Controlled release of antigens enhances immune response.
- **Antimicrobial Therapy:** Encapsulation of antibiotics improves efficacy and reduces resistance issues.

Diagnostics and Imaging

Microencapsulated nanoparticles can carry contrast agents for enhanced imaging techniques like MRI, CT, and PET scans.

Functionalized nanoparticles enable real-time tracking and diagnosis of diseases.

Wound Healing and Tissue Regeneration

Encapsulated growth factors or bioactive molecules promote wound healing and tissue repair. Effective in managing chronic wounds like diabetic foot ulcers.

Personalized Medicine

Enables tailored treatment by encapsulating drugs based on individual patient profiles. Supports the combination of multiple drugs for synergistic effects.

Reduced Toxicity and Improved Stability

Encapsulation protects sensitive drugs from environmental factors (e.g., pH, enzymes). Reduces systemic toxicity by preventing premature drug release.

Applications in Neurological Disorders

Crossing the blood-brain barrier (BBB) is possible with microencapsulated nanoparticles, making them suitable for treating conditions like Alzheimer's or Parkinson's disease.

Cosmetic and Dermatological Uses

Encapsulation of active ingredients for anti-aging, sunscreen, or therapeutic skincare products. Enhances penetration and effectiveness of active molecules in skin disorders.

Examples of Microencapsulated Nanoparticles in Medicine

Liposomal formulations: e.g., Doxil (doxorubicin for cancer therapy).

Polymeric nanoparticles: e.g., PLGA-based drug carriers.

Inorganic nanoparticles: e.g., silica or gold nanoparticles for diagnostics.

Hydrogel encapsulation: Sustained delivery of insulin or painkillers.



[6] CONCLUSION

Through this review paper it can be concluded that encapsulation is a method of covering an active compound with an inert coating to protect it and enable control release of the active ingredient. Encapsulation is of two types; Microencapsulation and Nano encapsulation. In this paper the concept of micro encapsulation of nanoparticles is discussed. Nanotechnology assigns curative agents at the nano scale level while developing nano medicines that are utilized in target delivery and control release types of drugs. Nano materials have the size range between 1 and 100 nm. Microencapsulation is a process of encapsulating an active nanoparticle drug with an inert micro level covering. There are many techniques through which microencapsulation is done, these techniques are; coacervation, cyclodextrin inclusion, emulsification, extrusion, fluidized bed coating, spray cooling and spray drying. Micro encapsulation of nanoparticles have many advantages such as increase in bioavailability of the active compound, prevention of toxicity, enhanced stability and pharmacological activity, control release and protection from physical and chemical degradation. The microencapsulated nano particles find use in various industries like pharmaceutical industry, cosmetic industry, food and agriculture industry. Although many studies show the utility of microencapsulation in nanoparticles, to understand the method better more extensive research is required in this area so that better and comprehensive conclusions can be drawn and this technology can be utilized in an optimum way.

[7] AUTHOR(S) CONTRIBUTION

The authors agreed to have no connections or engagements with any group or body that provides financial and non-financial assistance for the topics and resources covered in the article.

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[10] PLAGIARISM POLICY

The authors declare that any kind of violation of plagiarism, copyright, and ethical matters will be handled by all authors. Journalists and editors are not liable for the aforesaid matters.

[11] CONFLICT OF INTEREST

The authors declared that no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

[12] PROTECTION OF RESEARCH PARTICIPANTS

This study do not involve any such criteria or condition.



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