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A Literature Review Of Nanocarrier Development Through Emulsification Diffusion Method (Edm)

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ABSTRACT

An overview of the development of nanocarriers is presented in this work using the practical technique of the Emulsification Diffusion Method (EDM). The field of nanomedicine, which combines nanotechnology and medicine, involves creating new therapeutic and diagnostic modalities by employing precisely designed substances with this range of lengths. Many medicinal products and diagnostic tools based on nanoparticles have been developed. The emulsification-diffusion method (EDM) was utilized to prepare nanometer-sized particles, which are commonly used as polymeric carriers. The process involves emulsifying a drug and polymer solution in an aqueous phase that has been saturated with stabilizers and then adding an excessive amount of water. Investigations into how process variables affect the average size of nanoparticles have been carried out. It was made apparent that the kind and concentrations of stabilizer, the speed at which the magnetic stirrer homogenizes, and the polymer concentration all affected the size of the nanoparticles. Additionally, the medications integrated into nanocarriers have a longer half-life in circulation, which boosts their effectiveness and allows for a lower application dose. Because of their small size and high surface area, drug nanocarriers are also more bioavailable and soluble, which allows their many atoms and high surface energy to act as catalysts.

Keywords: Nanocarrier,Diffusion,Bioavailability,Solubility,Catalysts.

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1. Introduction:

Nanotechnology is the study of extremely small-scale phenomena. It entails the small-scale use and alteration of materials. Because of the differences in how atoms and molecules behave at this size, there are many fascinating and unexpected applications that can be made. Within a wide range of product domains, studies on nanotechnology and nanoscience have emerged rapidly in recent years. It offers chances for material development, including medical applications, where traditional methods might run out of steam. It is incorrect to think of nanotechnology as a single method that has limited application. Nanotechnology is more than just extremely small structures and products, despite its frequent designation as the "tiny science." Large surfaces and bulk materials frequently contain features at the nanoscale. The design, synthesis, and application of materials at the atomic, molecular, and macromolecular scales constitute nanotechnology, which aims to produce new materials at the nanoscale. Drug carriers that are solid and submicron-sized (less than 100 nm in diameter) and have the potential to biodegrade are known as pharmaceutical nanoparticles. A mixture of nanosphares and nanocapsules is referred to as a nanoparticle. As opposed to nanospheres, which are matrix systems with uniform drug distribution, nanocapsules have a unique polymeric membrane enclosing the drug. Successful drug delivery systems have previously been implemented using nanoparticles. Nanoparticles are one of the main instruments in nanomedicine and offer enormous benefits in terms of drug delivery and targeting. They can also be used to combine therapy and diagnosis. Topics include bioresponsive triggered systems, systems interacting with body smart delivery, nanochips for nanoparticle release, carriers for advanced polymers for the delivery of therapeutic peptides / proteins, control of sensitive drugs, function (of active drug targeting), biomimetic polymer architecture, and virus-like systems for intracellular systems. Iomimetic polymer architecture, virus-like systems for intracellular systems, control of sensitive drugs, function (of active drug targeting), bioresponsive triggered systems, systems interacting with body smart delivery, nanochips for nanoparticle release, and carriers for advanced polymers for the delivery of therapeutic peptides / proteins are among the topics included. To deliver or regulate the amount & rate, drug delivery techniques were developed. Most of the major, long-running internal research projects on delivery of drugs involve dispersions and formulations with nanoscale component parts (1). Polymeric nanocarriers are particles made of natural, semi-synthetic, or synthetic polymers. Many monomer units polymerize to form polymeric nano systems, which can self-assemble and organise into ananometric (10–100 nm) sizes under specific circumstances (2) (3). Drugs can be bound, entrapped, or encapsulated in a polymeric nanocarrier as a drug conjugate, nanosphere, or nanocapsule, depending on the manufacturing technique (4).

Nanocarrier and its objectives:

Nowadays, nano-based science and technology have shown remarkable progress in research and medicine applications. The dimension of nanostructured carriers, or particles, in pharmaceutical and medical science up to 100 nm in size is one of the core values of the nanotechnology approach. The nanostructured carriers need to be made

in such a way as to achieve maximum efficacy at the target sites with a precise, suitable dose and dosage form (5).

According to this definition, a nanocarrier's dimensions are: The total physical dimension(s) of a particle are determined by its atomic structure. Its effective size in a given matrix is based on its diffusion/sedimentation behavior, which can include the agglomeration or aggregation of other particles in the matrix as well as the potential adsorption of matrix constituents to the nanoparticle surface. Finally, its mass/electron distribution determines the effective size of the particle. The characteristics of bulk materials are largely determined by the surface atoms and surface energy because they have a much lower surface-to-mass ratio than nanoparticles (6).

Using physical dispersion or adsorption on the particle surface, colloidal particles known as nanospheres trap pharmaceuticals inside their matrix. In contrast, nanocapsules are systems consisting of a core cavity with an encapsulated drug and a polymeric shell surrounding it. Targeting ligands can be combined to create polymeric capsules that have improved intracellular drug delivery, enhanced selectivity for cancer cells, and decreased toxicity and side effects. Various ligands, including aptamers, peptides, monoclonal antibodies (mAbs) or antibody fragments, and small molecules like folic acid that are affixed to the shell-forming block, are frequently directed towards polymeric capsules (7)(8). To enable cellular selectivity and intracellular delivery of polymeric micelles, these ligands are specifically bound to antigens or receptors that are overexpressed on the cancer cell (9) . How well polymeric carriers modified with these ligands work depends on their density and binding capacity, which can enhance receptor internalization and drug biodistribution. A drug-polymer conjugate is created by a linker or spacer creating a chemical bond between the two (10).

Rationality of Nanocarriers in Drug Delivery:

Moreover, the high surface energy and high atom count of nanoparticles can have a major impact on catalytic performance. When formed as nanoparticles with a large surface area, catalytically inactive bulk materials can thus be converted into extremely active catalysts. A smaller number of orbitals is responsible for the formation of bands in a solid made up of fewer atoms. Alterations in the band structure are caused by this effect. Owing to these unique properties, nanoparticles are highly sought-after in an array of fields such as photovoltaic, biological and medical, gas and energy storage, catalysis, and optical and electrical devices. Because of this, there is increasing interest in nanoparticles, both in research settings and in consumer products, where they are already widely used. Different chemical forms, such as large biomolecules, metals (oxides), micelles, and synthetic polymers, can be converted into nanoparticles. There are numerous techniques for analysing the distinct chemistry present in each of these materials. However, a nanoparticle's behaviour is frequently primarily determined by its nanometer-scale dimensions. Consequently, the analysis of nanoparticle size, shape, surface charge, and porosity during the characterization process is an essential first step towards fully understanding and predicting their behavior. The dimensions of nanoparticles affect their ability to functionalize, fluid drag and diffusion, optical properties, and uptake into cells. A colloidal suspension's stability and

tendency to aggregate are controlled by surface charge, which also plays a significant role in influencing how well nanoparticles interact with their environment. Sub-nanometer precision in measuring the size and morphology of individual nanoparticles can be achieved through high resolution microscopy techniques such as electron microscopy or scanning probe microscopy. This provides remarkably detailed information on the shape of the nanoparticles being studied. The atomic structure or the scanning probe's reaction to the electron beam that impacts it is what these characterization methods depend on. Strategies like scanning electron microscopy (SEM) can be used to image the surface of the specimen by identifying secondary electrons that are released when the sample interacts with an incoming electron beam (6).

Drug nanoparticles exhibit enhanced bioavailability and increased solubility because of their high surface area and smaller size. Additionally, they have the ability to cross the blood brain barrier (BBB), enter the pulmonary system, and pass through the tight junctions of skin endothelial cells. In particular, nanoparticles composed of natural and synthetic polymers, both biodegradable and non-biodegradable, have attracted more attention because they can be customized for targeted drug delivery, improve bioavailability, and provide a controlled release of medication from a single adaptation—through system adaptation, the drug can be prevented from being degraded by endogenous enzymes (11).

Applications of Nanocarriers:

The application of carefully engineered materials at this length scale to create new therapeutic and diagnostic entities is the field of nanomedicine, which unites nanotechnology and medicine. Numerous nanoparticle-based therapeutic and diagnostic agents have been created to address a wide range of illnesses, including diabetes, cancer, pain, allergies, asthma, infections, and more. In addition to lowering therapeutic toxicity, extending the product life cycle, and ultimately lowering health care costs, these nanoscale agents may offer more convenient and/or effective routes of administration. When used as medicinal delivery systems, nanoparticles offer controlled release and targeted distribution. Molecular scale detection is made possible for diagnostic applications by nanoparticles. This aids in the discovery of anomalies not picked up by traditional diagnostic techniques, such as disease markers, precancerous cells, and virus fragments. It has also been shown that imaging contrast agents based on nanoparticles can improve the sensitivity and specificity of magnetic resonance imaging. The use of nanoparticles in drug delivery has many established benefits. Drugs that are poorly soluble in water are rendered more soluble, immunogenicity is decreased to extend the systemic circulation half-life of the drug, drugs are released gradually or in a way that adapts to the environment to minimize the frequency of administration, drugs are delivered in a targeted manner to minimize systemic side effects, and multiple drugs are delivered simultaneously for combination therapy to create a synergistic effect and inhibit drug resistance (12) (13).

The field of nanomedicine has attracted the attention of academic and industry researchers due to the recent achievements in nanoparticle therapy. Over the past ten years, there has been an increasing force driving the rate of discovery, leading to the creation of increasingly complex nanoparticle

systems. Although liposomes and polymeric conjugates are still the most commonly used nanoparticle platforms, other options include metallic, ceramic, polymeric, micelle, nanoshell, dendrimer, engineered viral, albumin-based, polysaccharide-based, and metallic nanoparticles. In nearly every area of medicine, including oncology, cardiology, immunology, neurology, endocrinology, ophthalmology, pulmonary, orthopaedics, and dentistry, these nanoparticles have demonstrated therapeutic promise. Biodegradable polymeric micelles have recently attracted a lot of attention as drug delivery nanocarriers due to their remarkable therapeutic potential. Polymeric micelles are created by the self-assembly of block copolymers, which are made up of two or more polymer chains with different levels of hydrophobicity. Such copolymers spontaneously assemble into a core-shell micellar structure in an aqueous medium to lower the free energy of the system. To be more precise, the hydrophilic blocks from the corona-like shell stabilize the core through direct contact with water, while the hydrophobic blocks form the core to minimize their exposure to aqueous environments. The ideal nanocarrier for medication delivery is provided by this micellar structure. Drugs can be loaded into its hydrophobic core very effectively, especially those that are poorly soluble. The micelle's hydrophilic shell provides functional groups suitable for additional micelle modification in addition to steric protection. Each polymeric micelle is much larger than a polymer drug conjugate, allowing for the storage and controlled release of a greater number of drugs. One of the several possible routes for drug release from encapsulated pharmaceuticals is drug diffusion through the polymer matrix; another is drug diffusion followed by polymer swelling; and a third option is surface erosion of the biodegradable polymers in greater amounts. The release of medications from polymeric micelles can also be brought on by environmental factors like temperature and pH variations. Environmental variables like temperature and pH changes can also cause the release of drugs from polymeric micelles. Whereas liposomes and other surfactant micelles are less stable in blood than polymeric micelles because some amphiphilic copolymers have a micelle concentration value that is much lower. Additionally, two or more medications with comparable or dissimilar water solubility can be co-delivered using these polymeric micelle systems. therapy, or to administer medications and/or radiation agents concurrently with one or more therapeutic modalities. Antagonistic ligands modify the surfaces of these micelles. To improve the specificity, efficacy, and decrease the systemic toxicity of a drug, it is possible to target its delivery and uptake by a subset of cells using peptides, small molecules, and nucleic acid aptamers (14).

Emulsification diffusion method (EDM):

Nanoparticles have become one of the most promising dosage forms when it comes to possible formulations for drug delivery systems that are site-specific and involve drug targeting. The application of particle formation made from polymers has drawn particular attention. Following the completion of the drug release, these polymers do not need to be surgically removed. Polymer-based nanoparticles were successfully synthesized by us using the emulsification diffusion technique. The work presented here aimed to identify the ideal formulation parameters for the synthesis of drug-loaded nanoparticles at a size that could be

The technique known as spontaneous emulsion diffusion involves dissolving a polymer in a mixture of solvents, one of which is water immiscible and the other of which is miscible, in order to create biodegradable nanoparticles. This solution dissolves quickly in the miscible solvent, forming a nanoemulsion when added to an aqueous phase. The immiscible solvent evaporates, forming nanoparticles in the process. Initially, the nanoemulsion is generated by the interfacial turbulence that arises from the solvent displacement of the miscible solvent. This is an important reminder that there is no true diffusion step. As a result, this process can be viewed as a hybrid of the displacement and solvent evaporation processes. Given that it just employs miscible solvents, the modified spontaneous emulsification solvent method is undoubtedly a solvent displacement method. The terms "solvent quenching," "self-emulsifying solvent diffusion," "emulsification-solvent diffusion," "emulsion solvent diffusion and emulsified solvent diffusion," and "water-in-oil emulsification-diffusion" are interchangeable with those used in some scientific articles and patents (16).

General procedure for the formation of nanocarriers through the Emulsification Diffusion Method (EDM):

In order to form nanoparticles, two phases were identically saturated to produce a uniform mixing. Both liquids are in a thermodynamic state, with the organic phase containing polymers and suitable solvents and the water phase containing water and stabilizers. (FIGURE-1)

(i) After stirring causes the solvent solution to disperse as globules in equilibrium with the continuous phase, a significant interfacial area is created on which the stabilizing agent is subsequently adsorbed.

(ii)Water introduces an unstable element into the system.

(iii)It is responsible for the solvent's diffusion to the external phase. New nanoscale globules are formed during this solute transport process, and they progressively lose solvent;

(iv)Consequently, a new, continuous non-solvent phase appears, which causes the polymer of the globules to aggregate (15).

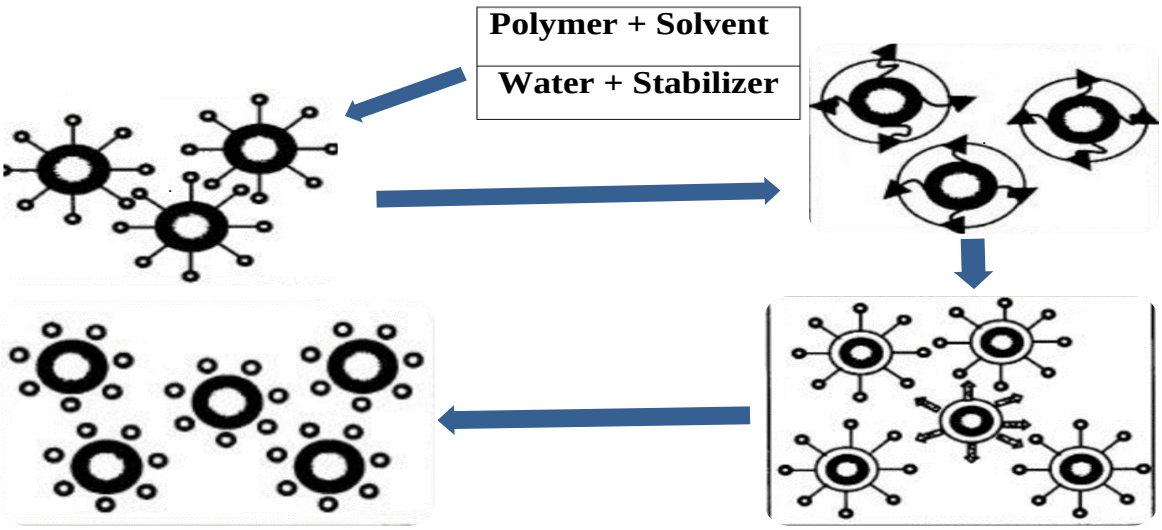

Figure 1 shows a schematic illustration of how nanoparticles are created using the emulsification–diffusion method (EDM).

Mechanism of action of the emulsification diffusion method (EDM):

Step one involves gradually saturating both the water and the partially water miscible solvent. This procedure is carried out to stop the polymer and stabilizer from quickly aggregating when the solvents are in proximity. A new patent showed that using tri-ethyl citrate as a solvent did not require saturation in order to produce medication nanoparticles. The organic and aqueous phases are then formed, respectively, by dissolving the polymer(s), drug(s), and stabilizer(s) in the saturated solvent and water, respectively. Oils are a component of the organic state if and when nanocapsules are formed. Next, a stable oil-in-water emulsion is created by uniformly combining the organic and aqueous phases. The typical organic/aqueous volume ratio is 1:2. Conventional mechanical stirrers can be used for the dispersion process; however, various patents have suggested the use of ultrahigh pressure, high pressure homogenizers, and sonication as alternative dispersion methods. It is crucial to keep in mind that, according to the formation mechanism, creating a nanoemulsion is not required in order to produce nanoparticles. Among the several sugars and excipients investigated for freeze-drying, trehalose and sucrose, or a mixture of these, appear to be the most commonly utilised and effective cryoprotectants. It is imperative to acknowledge that the lyophilisate that is reconstituted needs to exhibit physicochemical and performance characteristics that are either on par with or better than those of the initial suspension. Sometimes, in order to reach the dispersion size without particles resulting from microaggregation or undispersed particles formed during drying, cryoprotectants must be used. Using the classic emulsification-diffusion method, a variety of active ingredients have been encapsulated, including ciprofloxacin, tacrolimus, temozolomide, dragon's blood, etc. A few of these compounds have even been granted patents for specific medical purposes. Biodegradable activated nanoparticles for targeted drug administration can be produced using this technique. The targeted agent is applied to the nanoparticle's outer surface using the formulation that the inventors designed. It is constituted of a biocompatible polymer that is not covalently bonded to any other polymer and a spacer compound consisting of at least one electrophile that selectively reacts with any nucleophile on the targeted agent. An active agent is present inside or outside of a biodegradable nanoparticle. One component of the organic phase is the drug (such as curcumin or another potent anti-cancer agent), and one component of the aqueous phase is the spacer. Intriguing ideas include a composition that can be employed in a targeted medication delivery system that concentrates magnetic nanoparticles on a target using a magnetic field, and a technique for manufacturing magnetic nanoparticles based on the emulsification diffusion process. More specifically, a medicine, a magnetic material, and magnetic nanoparticles encased in biodegradable synthetic polymers are present in the mixture. An essential component of getting ready for the emulsion diffusion approach is learning how to induce diffusion. Water that has been diluted is added to create dispersions that have little solid content. It was therefore suggested to employ direct solvent distillation to remove a low boiling point solvent from the internal phase and transfer it to the exterior phase in light of the formation

mechanism. Polymers have patented an analogous emulsification-diffusion method for producing nanoparticles. Owing to saturation, the continuous aqueous phase is rich in solvent, so when it rapidly separates, in an anti-solvent media created by solvent globules freely flowing to the continuous phase, the material will clump together as nanoparticles. The addition of surplus water dilutes the emulsion. This type of emulsion can be employed inverted to create hydrophilic polymer nanoparticles or encapsulate medications that dissolve in water using a water-in-oil system. The production of nanoparticles will occur as a result of interfacial phase changes of the polymer during diffusion. When predicting the elements and circumstances that decide whether the procedure will succeed or fail, as well as when adjusting the preparative conditions to maximize the outcomes, an understanding of nanoparticle formation is crucial. In summary, it is commonly recognised that an emulsion droplet is usually produced when oil and water are emulsified via traditional mechanical shear, barring unusual circumstances. Strong correlation should be expected since after the solvent is withdrawn, one polymer particle should develop in each emulsion droplet. With the emulsification diffusion approach, this isn't the case though. It is clear that diffusion-related interfacial processes aid in the globule's division into nanodroplets before particles form. The emulsification-diffusion process cannot be explained by the interfacial turbulence mechanism, which is used to clarify how nanoparticles are created through nanoprecipitation. In the case of nanoprecipitation, for example, the solvent is completely miscible with water, despite the fact that the solvent properties are different. However, the emulsification diffusion method's partially water miscible solvents only cause a small amount of interfacial instability—not enough to cause spontaneous emulsification. To ensure that nanoparticles develop, a sizable interfacial region needs to form in the emulsion As a result, solvent transport is critical to the creation of nanoparticles when using the emulsification-diffusion approach (16).

API (Active Pharmaceutical Ingredients) used as a model drug:

Silica is added to pharmaceutical formulations to improve their flowability when taken orally. Solid dispersions become more wettable, which accelerates the rate of dissolution. Hydrophilic lipid-based compounds and other excipients that enhance drug release control work in this way. To reduce the rate at which the therapeutic agent releases, a water-insoluble polymer can be incorporated into the solid. This is a subset of polymers used in the pharmaceutical industry, such as eudragits, which have properties relevant to therapeutic applications, such as water permeability, which permits the drug to permeate into the supporting medium. To decrease the pace at which the therapeutic drug releases, a polymer that is soluble in water can be added to the solid formulation. For instance, Naproxen ($C_{14}H_{14}O_3$) is a non-steroidal anti-inflammatory medication belonging to the Class II family. Its bioavailability is restricted by its dissolution. Frequent uses include the treatment of mild to moderate pain, fever, stiffness, and inflammation. However, in some patients, it can induce gastrointestinal problems (17). The therapeutic action of naproxen is usually linked to GI adverse effects. Despite the possibility of gastric toxicity, many NSAIDs have good cardiac profiles. It is known that NSAIDs inhibit the cyclooxygenase (COX) enzyme.

The higher PGE2 concentration in inflammatory tissues is caused by NSAIDs in addition to cancer cells. Naproxen demonstrates antipyretic, analgesic, and anti-inflammatory properties (18). A maximum daily over-the-counter dose of 440–660 mg is permitted by local regulatory bodies for non-prescription dosing, which should occur every 8–12 hours. This dose regimen is different from the prescription one, which typically calls for taking 500 mg two to three times a day up to a maximum of 1500 mg daily. Naproxen is a superior comparator in many clinical trials due to its excellent analgesic properties and long half-life, which guarantee steady blood levels and efficacy. In order to optimize therapeutic activity and reduce the likelihood of side effects, NSAIDs must be distributed locally in injured tissues (19). Naproxen exhibits high protein binding (> 99.5%); nevertheless, the free fraction experiences a notable increase with elevated plasma concentrations. Naproxen's volume of distribution is relatively small, approximately 10% of body weight. The medication enters the synovial fluid and membrane with ease (20). The benefits of microemulsions for drug delivery via transdermal application have been attributed to three predominant mechanisms. First, the high solubility potential of hydrophilic and lipophilic drugs in microemulsion systems may raise their thermodynamic activity in the direction of the skin. Second, the microemulsion's permeation enhancer ingredients may damage the stratum corneum's structure and promote drug penetration through the skin. Third, because a drug's affinity for the internal phase of a microemulsion can be readily changed to favor partitioning into the stratum corneum, thereby altering its portion in the microemulsion, the drug's permeation rate from the microemulsion may be increased (21). Nanosensors exhibit promising mass production prospects at a comparatively low cost, along with good reproducibility concerning size homogeneity. In addition to quantitative analysis, they are used in many other fields, such as screening. Luminescence, which can detect both fluorescence and phosphorescence, is typically the property that optical sensor nanoparticles use to measure the recognition process. Recent research endeavors have resulted in the creation of novel approaches for the synthesis of nanoparticles through distinct pathways. These include the radical polymerization of weakly water-soluble monomers like styrene or methacrylates in miniemulsion polymerization; the spontaneous formation of nanoparticles; and emulsion polymerization, which is limited to the radical polymerization of small, uniform, and stable precursor droplets to the final polymer dispersion (22) .The degree to which the drug has been incorporated into the system and the way the drug and polymer interact are crucial elements that influence the release profile (23).

Due to the potential for GI mucous damage, that effect exacerbates the situation. Drug nanoencapsulation offers a potential solution to prevent gastrointestinal side effects caused by drug molecule contact with the GI mucosa. Different NSAIDs can be nanoencapsulated to reduce upper gastrointestinal damage because the drug will not come into contact with the mucosa. Additionally, the drug may become less toxic, dissolve more readily in water, have a faster onset of action, or be more permeable through biological membranes. Since the discovery of mesoporous materials (MSN), which have been shown to have potential in various areas of application, the majority of

studies involving them have concentrated on optimizing their synthesis with the aim of controlling the properties of the nanoparticles that are formed. Stable dissolution, pore size and volume, uniform size of the nanoparticles, and their shape are, in general, the controlled parameters of greatest interest. The reproducibility and knowledge of pore size dictate the kinds and amounts of molecules that can be loaded into their interiors. Consequently, mesoporous nanoparticles are of biomedical interest and are typically used for therapeutic purposes because they increase the solubility of poorly soluble drugs, allowing for the controlled, sustained, or release of the drug in response to stimuli, adhering to different biological systems, and shielding the drug from organism degradation. Its use as catalysts and diagnostic agents is also included in its application. In general, they show a lot of promise for drug release (24) .

Factors that influence Emulsification Diffusion Method (EDM):

The formation of nanoparticles and the impact of various preparative factors can be explained by a process known as "diffusion and stranding." This mechanism is not mechanically unstable; rather, it involves chemical instability. When the solvent is slowly introduced into water from an oil-solvent solution, some oil is also dissolved into the water by the solvent. As a result, immediately at the interface, the water splits into three phases. The related oil is liberated from the solution and becomes "stranded" as microscopic emulsion droplets when the solvent diffuses further into the water. The emergence of local supersaturation zones during diffusion in one or both phases is one factor contributing to this kind of spontaneous emulsification. That being said, these starting mixtures are not saturated. It is suggested that phase transitions in these regions give rise to emulsion droplets, indicating the short-lived nature of such supersaturation. Furthermore, supersaturation in the vicinity of an interface may encourage the breakdown of a unique yet connected chemical instability mechanism. The breadth of this "diffusion-stranding" mechanism explains well why the emulsification-diffusion method can yield nanoparticles. Diffusion of the solvent transports the polymer molecules from the globules to the aqueous phase, according to the basic principle, forming localized supersaturation zones where new globules or partially desolvated polymer aggregates may be formed. These aggregates must be stabilized with a stabilizer present in order to prevent them from consolidating and forming large particles. After the solvent has completely diffused from the droplet, polymer consolidation in the form of nanoparticles will occur. Since an oil dissolves with the polymer in nanocapsules, another useful model in this case is the diffusion-stranding mechanism. Because of this, there are localized supersaturated regions in the aqueous phase where oil and polymer molecules are diffused from the globules by solvent. This kind of breakdown of supersaturation results in the formation of nanodroplets, which rapidly stabilize, from the blend comprising the oil, polymer, and any residual solvent. After the polymer molecules inside the oil nanodroplets consolidate on the interface between the new phases (oil/aqueous phase) generated by solvent diffusion, both of which are nonsolvent for the polymer, the oil nanodroplets finally form a thin film around them. The type of particles obtained by the emulsification-diffusion process is generally satisfactorily explained by this

mechanism, and it is linked to the characteristics and transformation of the supersaturated zone. The concentration and type of stabiliser, drug, and biodegradable polymer; the amount and kind of diffusion medium; the rate of stirring; the ratio of oily to aqueous phases; the viscosity of the external phase; and other factors are the main variables that influence the process and, subsequently, the particle size (16).

Particularly for nanocapsules, significant effects were noted on size distributions, as well as the organic phase's solvent volume and the organic phase's polymer to oil ratio. There was a clear correlation between the size variation and the polymer in the organic phase, and it was inversely proportional to the solvent volume. The concentration of polymer also affects the thickness of the membrane of the nanocapsule. High molecular weight polymer chains have the ability to slow down a solvent's rate of diffusion during dilution. It is an interesting finding, this. Particle size will increase and the supersaturation layer will thicken as a result. Response surface methodology was used to optimize the emulsification diffusion process of biodegradable nanocapsules (25).

Rationality of using emulsification diffusion method (EDM):

Emulsification is the primary unit operation used in this method. To ensure a large superficial area for the diffusion stage and to create nanoparticles, a stable dispersion must be made accurately. If this is feasible, the formulator will determine how much HLB is needed to prepare a suitable dispersion. To create emulsion, the pharmaceutical sector now uses conventional mechanical stirrers. Submicronic particles can be captured by globules smaller than 100nm because solvent diffusion produces several nanoparticles within each emulsion droplet. (26).

Besides, The Emulsification-diffusion method comes up with numerous advantages: It is highly reproducible and efficient, (i) compatible with standard laboratory equipment, (ii) able to use solvents approved by pharmaceutical companies, (iii) solvent recycling possible, (iv) easily scaled up to a large scale. However, a key premise of this process is that low solid concentration dispersions are generated because of the large dilution required for the solvent to diffuse (27).

Conclusion

This analysis makes it clear that nontechnology application in medicine and medication delivery has created new avenues and opened several opportunities for the provision of safer, more individualised treatment options. The process of creating nanoparticles was supposed to be connected to the globule size reduction brought on by the solvent's quick diffusion. There are numerous known advantages to using nanoparticles in medication delivery. It improves the solubility of poorly water-soluble medications, releases the medication gradually or in a way that adjusts to the surroundings to reduce the frequency of administration, targets the medication delivery to minimize systemic side effects, and simultaneously delivers two or more medications for combination therapy to reduce drug resistance and maximize synergistic effects.

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