



INTERNATIONAL JOURNAL OF ADVANCE RESEARCH, IDEAS AND INNOVATIONS IN TECHNOLOGY

ISSN: 2454-132X

Impact factor: 6.078

(Volume 6, Issue 4)

Available online at: <https://www.ijariit.com>

Advancements in controlled Drug Release Systems

Akanksha Pradhan

akanksha.pradhan1901@gmail.com

Indian Institute of Technology, New Delhi, Delhi

Saksham Rawal

saksham.rawal99@gmail.com

Indian Institute of Technology, New Delhi, Delhi

ABSTRACT

There is a prevailing problem of a drug overdose, due to the sudden release of medicines in the body. It is challenging to provide a precise drug release rate. But microencapsulated drugs and 'active-gel' mixtures continue to provide us with better solutions in the field. In this review, we discuss both of these methods briefly, including why they are advantageous over standard drug delivery procedures and what is the need for further research in this area.

Keywords: Drug delivery, Microspheres, Micro-encapsulation, Rate of Drug Release, Active-gel, Hydroxy-Gel

1. INTRODUCTION

The process of drug delivery has had many advancements in the pharmaceutical industry. One such method is to form microencapsulated microspheres, which have the provision of controlled drug release when injected/orally taken. One such method is the microencapsulation process. The formation of the microsphere process is very crucial since its purpose is to release the exact amount of drug, with a very specific release rate. Formation of such microspheres generally uses the method of emulsification followed by solvent extraction/evaporation process. The emulsion contains the polymer, solvent, the API (Active Pharmaceutical ingredient) and the surfactant. The solvent in this emulsion is then extracted to form solid microspheres, with a certain amount of residual solvent. This study is a brief review of the microsphere formation process, focusing more on the solvent extraction step. A research about a new drug delivery method is also discussed, which uses an active gel, essentially a hydrogel-oil mixture.

2. MICROENCAPSULATION

Microspheres are drug delivery systems which can provide controlled/prolonged drug delivery. It is helpful when we need to target a drug to a specific site at a fixed rate, predetermined. They are free-flowing powders, generally made from polymers like PLGA. Their size range is 1 to 1000 micrometers. They play an essential role in the pharmaceutical industry. Microspheres have various characteristics. Ideally, they can incorporate a much high concentration of the drug. They are stable in nature, therefore have a high shelf life. The size of the Microsphere can be modulated, and they can quickly disperse in aqueous carriers, for injection). They are biocompatible and can be chemically modified.

With such characteristics, microspheres have considerable advantages over other drug delivery systems. Some of the benefits are they provide a prolonged and constant therapeutic effect. The solubility of a poorly soluble drug can be enhanced, by particle size reduction. Its use eliminates toxic side effects for overdosage or error/inconvenience of repeated injections. It is also advantageous as we convert the liquid to solid form to mask the taste. But with advantages, there are some disadvantages too, like the effective cost are higher than the standard formulations. The polymer used for the microsphere matrix and its effect on the body reduces the set of polymers to choose from. Since the microspheres are injected in our body, it is not a controlled environment. The stability of those microcapsules might be influenced as there might be changes in pH, temperature, etc.

The formation of Microsphere in the pharmaceutical industry goes through various stages. Some of the commonly used processes for microencapsulation are Single Emulsion method, Double Emulsion method, Phase separation and coacervation, solvent extraction, solvent evaporation, polymerization, and spray drying method. Figure 1.1 shows the flow diagram showing the formation of PLGA based microspheres by one such process. It involves emulsification followed by solvent extraction, solvent evaporation and drying.

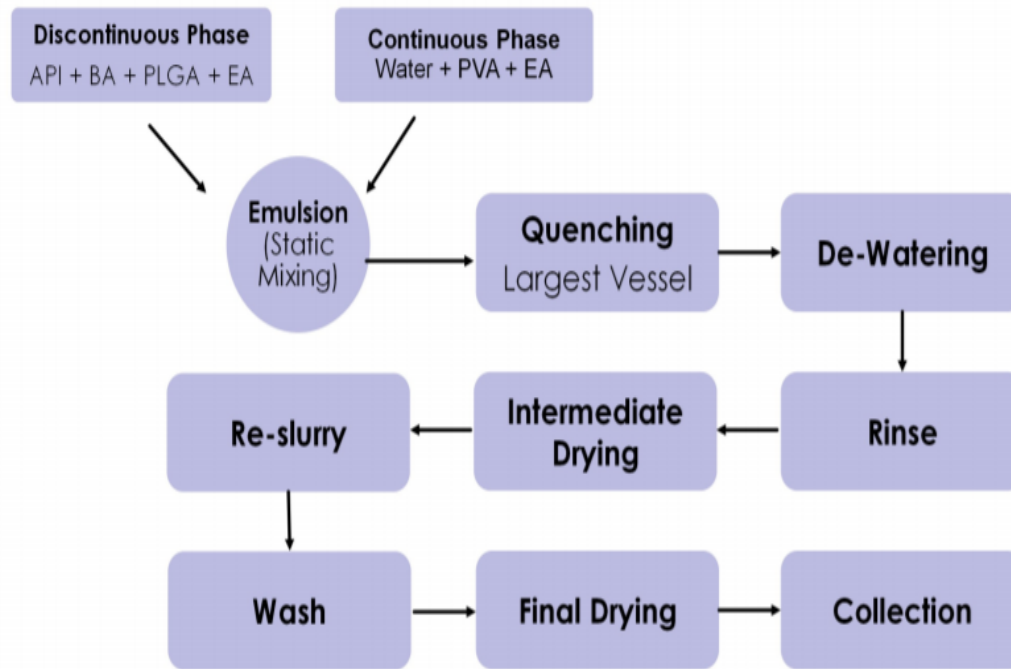


Figure 1.1 Microsphere formation process

3. DRUG RELEASE MECHANISM

The Drug release mechanism of the Microsphere follows Diffusion, Erosion, Dissolution and Osmosis.

Diffusion is the most common mechanism involved in drug release. There exists a dissolution liquid, dissolving to the core and making it leak out through pores or interstitial channels. The drug release obeys Higuchi's equation:

$$Q = [D / J (2A - \epsilon C_s) t C_s]^{1/2}$$

Q is amount of drug released per unit area of exposed surface in time t;

D is diffusivity of solute in solution;

A is amount of drug per unit volume;

C_s is solubility of drug per unit volume;

ε is the porosity of microcapsule wall;

J is tortuosity of capillary system in wall

The equation can be simplified to the form: $Q = vt$, where v is the apparent release rate

Drug release is sometimes caused by Erosion of coat, due to enzymatic/pH hydrolysis. It works for only certain materials like bee's wax and glyceryl monostearate.

Osmosis can also be a probable cause for drug release when an osmotic pressure difference between inside and outside of the polymer coat. The coat sometimes behaves like a semi-permeable membrane, hence causing such effect.

If the coat is soluble in the dissolution fluid, then the rate of its dissolution determines the release rate of the drug in the core. Here, the influencing parameters are thickness and solubility of the polymer in dissolution fluid.

The modelling of the drug release profile lacks research, and it is complicated because the microparticles have a size range, they vary in size as well as shape, the arrangement of the core and coat materials; making the sample too random. This variation also causes all physiochemical properties to be different, thus making the modelling difficult. However, some generalization can be made regarding the release characteristics:

From microcapsules conforming to reservoir type, the release rate is of zero order. Monolithic type microcapsules have release rates which are t_{1/2} dependent for the first half of the total drug release. The release rate declines exponentially after that. However, if a there is a monolithic microcapsule is dissolved drug in excess, the release rate is always t_{1/2} dependent.

4. OIL-HYDROGEL MIXTURE

The problem of drug overdose has been in the medical health industry since the beginning.

With such diversity and types in health profile, it has been difficult to provide with the exact rate of drug to be released and administered in the cells of thousands of patients. Searching for methods administering active agents at a fixed rate has been a vast area for research among pharmacologists. The required proteins or other substances present in the form of tablets, ointments or

injections are usually released very quickly into the body; which increases the risk of that being a case of overdose. The effect is not as efficient as intended as the time duration is shortened by the rate of release. Thus, these kinds of methods involving drug release over a long time and at a constant rate are rare and generally very complicated to fabricate.

While studying about the origins of life, Professor Job Boekhoven, together with his team of students from the Technical University of Munich, investigated how the molecules combined to form the precursors of the first living cells in the earliest period of the Ocean's existence.

The ability of the molecules to protect themselves from degradation was studied through experiments, majorly involving oil droplets. After the study, it was found that the unstable molecules could survive for much more extended time when they had the ability to form oil droplets. If the molecules couldn't form oil droplets around them, they degraded faster. It was suggested that these droplets could be protecting the cells or the molecules inside of them.

However, the oil shield, which the molecules can form around themselves, is permeable; that is, it does not completely prevent the transfer of any material in or out. As it turned out, hydrolysis of the shield took place with the surrounding water. The reaction causes the oil droplets to shrink and disappear slowly by continuously losing mass. This paved the way for the idea of using the constant decay process of the "Active Droplets" in the field of drug dosage.

It was found that the oil droplets released the encapsulated drug continuously while their size got smaller. Consequently, the drug release rate remained constant for the entire time the drug was released (release period). This approach is very straightforward, making it very powerful. Only three components are needed: any drug that separates in the oil, droplets made of an oil that is hydrolysable, and a hydrogel to stabilize the position of the droplets in the medium. The active substances in the oil droplets can be loaded in small or large doses into the oil droplets. They are released as soon as the surface of the droplet comes in contact with the water present in the blood or tissue. The oil hydrogel mixture allows the released active substances or agents to be administered continuously. We can also predetermine the rate at which the agents dissipate entirely into the surroundings, by the hydrolysis process.

This phenomenon has many potential fields of application. If scaled up, it could reduce the problem of drug overdose to zero, making the medication process more precise and effective. One of the possible applications could be in case of disinfectants. Healing-promoting sore pads can also have such mixtures to treat poorly healing wounds. The team has applied a patent for the oil-hydrogel mixture.

5. CONCLUSION

These microfabricated systems and active gel mixtures offer a lot of advantage over standard delivery systems. The process of their drug delivery is unique and can be tailored to target specific tissue systems. Although there have been many advancements made in this field, there are many challenges like the modelling of the drug delivery for both of the systems, making the technology cost-effective, since the microcapsule drugs are substantially costlier than the conventional medicines. Particularly the use of cheaper biopolymers is encouraged. For the development of a safe and efficient system will require in-depth investigations in technological as well as biological aspects.

6. REFERENCES

- [1] Aggarwal, Geeta & Nagpal, Manju. (2018). Pharmaceutical Polymer Gels in Drug Delivery. 10.1007/978-981-10-6080-9_10.
- [2] Kadam N. R. and Suvarna V (2015), MICROSPHERES: A BRIEF REVIEW
- [3] Birnbaum DT, Brannon-Peppas L. Microparticle drug delivery systems. In: Brown DM, editor. Drug delivery systems in cancer therapy. Totowa: Humana Press Inc; 2003. P. 117-136.
- [4] BAL T. Design and development of the sustained release mucoadhesives microspheres of montelukast using jackfruit latex. M.Pharm [Thesis]. Dibrugarh Assam: Dibrugarh University; 2005.
- [5] Berkland C, Kipper MJ, Narasimhan B, Kim KY, Pack DW. Microsphere size, precipitation kinetics and drug distribution control drug release from biodegradable polyanhydride microspheres. *J Control Rel.* 2004;94:129-141.
- [6] Ike O, Shimizu Y, Wada R, Hyon SH, Ikada Y. Controlled cisplatin delivery system using poly(D,L-lactic acid). *Biomaterials.* 1992;13:230-234.
- [7] Singh, M.N. & Yadav, Hemant & Ram, M & Shivakumar, H.G.. (2010). Microencapsulation: A promising technique for controlled drug delivery. *Research in pharmaceutical sciences.* 5. 65-77.
- [8] Hombreiro PM, Zinutti C, Lamprecht A, Ubrich N, Astier A, Hoffman M, *et al.* *The preparation and evaluation of poly(epsilon-caprolactone) micro-* M.N. Singh *et al.* / *RPS 2010; 5(2): 65-77*