Journal of Medicine and Biology

Review Article | Vol 1 Iss 1

Preparation and Evaluation of Aspirin Loaded Microspheres by Solvent Evaporation Technique

E Veena Rani and A Krishna Sailaja*

RBVRR Women's College of Pharmacy, Osmania University, Hyderabad

***Corresponding author:** A Krishna Sailaja, RBVRR Women's College of Pharmacy, Osmania University, Hyderabad; Tel: 0402756 3065; E-mail: shailaja1234@rediffmail.com

Abstract

The aim of the present investigation is to prepare aspirin loaded microspheres by solvent evaporation technique. The drug and Ethyl cellulose polymer were dissolved in acetone under stirring at 700 rpm. The aqueous phase containing a surfactant was kept under stirring. Then the organic phase was added to the aqueous phase under continuous stirring. The obtained microspheres were evaluated for product yield, Drug content, entrapment efficiency and loading capacity. The SEM images clearly reveals that the particles were found to be spherical in shape. The product yield, drug content, entrapment efficiency and loading capacity was found to be 90.6%, 85.3%, 23% and 4.1% respectively.

Keywords: ***Evaporation technique; Polymer; Drug content***

Received Date: May 23, 2019; **Accepted Date:** June 22, 2019; **Published Date:** June 29, 2019

Introduction

Microspheres are identified as the free-flowing powders made of protein or synthetic polymers which are biodegradable in nature and ideally having a particle size less than 200 µm [1,2]. Some of the chronic diseases required frequent administration of the drug to efficiently deliver the drug for a prolong period of time. Patient compliance will get reduced because of frequent administration of the drug. To overcome the above problems, different types of controlled release formulations are developed, so that patient compliance is increased through prolonged effect, adverse effect decreases by lowering peak plasma concentration. The controlled release formulations maintain relatively constant levels of drug in the plasma by releasing the drug at a predetermined rate for an extended period of time [1,2].

One such in Microspheres as carriers of drug become an approach of controlled release dosage form in novel drug delivery system. Generally, microspheres are termed as "Monolithic sphere or therapeutic agent or made of a continuous system containing one or more polymers in which the drug is dispersed uniformly. It has a particle size of (1-1000nm) [3,4].

Citation: E Veena Rani, Preparation and Evaluation of Aspirin Loaded Microspheres by Solvent Evaporation Technique. J Med Biol 1(1): 27-32.

Advantages of microspheres

- Increase bioavailability
- Enhanced patient compliance
- Effective targeting of the drug to the specific site and also maintains the therapeutic concentration of drug without any disturbances.
- Reactivity of the core is reduced in relation to the outside environment.
- The size, surface charge and surface hydrophilicity of microspheres are considered to be the important parameter for identifying the fate of the microspheres.
- Volatile core material has reduced evaporation.
- Bitter taste masking.
- GIT has been protected from irritant effects of the drug.
- Biodegradable microspheres are more advantageous than the large polymer implants because they do not require surgical procedures for implantation and removal.
- Controlled release delivery biodegradable microspheres are used to control drug release rates thereby decreasing toxic side effects, and eliminating the inconvenience of repeated injections.

Classification of polymers

Microspheres used usually are polymers. They are classified into two types i.e. synthetic and natural polymers [5].

Synthetic polymers: It is divided into two types.

a. Non-biodegradable polymers *e.g.* Poly methyl methacrylate (PMMA), Acrolein, Glycidyl methacrylate, Epoxy polymers.
b. Biodegradable polymers *e.g.* Lactides, Glycolides & their co polymers, Poly alkyl cyno-acrylates, Poly anhydrides.

Natural polymers: It is obtained from different sources like proteins, carbohydrates and chemically modified carbohydrates.

a. Proteins: Albumin, Gelatin, and Collagen.
b. Carbohydrates: Agarose, Carrageenan, Chitosan, Starch.
c. Chemically modified carbohydrates: Poly dextran, Poly starch.

Types of Microspheres

Bio-adhesive microspheres: Adhesion can be defined as sticking of drug substance to the biological membrane by using the adhering property of the polymers. Adhesion of drug to the mucosal membrane such as buccal, ocular, rectal, nasal etc. can be termed as bio adhesion. Such type of microspheres exhibits a prolonged residence time and causes intimate contact with the membrane and produces better therapeutic action [6].

Magnetic microspheres: It is a type of delivery system in which localization of the drug to the target site is achieved. In this system larger amount of freely circulating drug can be replaced by smaller amount of magnetically targeted drug. Magnetic carriers like chitosan, dextran etc. receive magnetic responses to a magnetic field from incorporated materials [6].

Therapeutic magnetic microspheres: They are used to deliver chemotherapeutic agent to liver tumour. Drugs like proteins and peptides can also be targeted through this system.

Diagnostic microspheres: This technique is used for diagnosing liver metastases and also to distinguish bowel loops from other abdominal structures by forming nano-size particles supra magnetic iron oxides.

Floating microspheres: In this floating type, the bulk density is less than the gastric fluid and so that the microspheres remains buoyant in stomach without interfering with the gastric emptying rate. The drug is released slowly at the desired rate, if the system is floating on gastric content increases gastric residence and causes fluctuation in plasma concentration. Moreover, it also reduces chances of striking and dose dumping and it is a technique by which the therapeutic effect is improved and also reduces the dosing frequencies. Ketoprofen is a type of drug which is given in this form.

Radioactive microspheres: Radio embolization therapy microspheres sized 10 nm - 30 nm are of larger than capillaries and gets tapped in first capillary bed when they come across. They are injected to the arteries that lead to tumour of interest. So, in all these conditions radioactive microspheres deliver high radiation dose to the targeted areas without effecting the normal surrounding tissues. It differs from drug delivery system, as radio activity is not released from microspheres but acts from within a radioisotope typical distance and the different kinds of radioactive microspheres are α emitters, ß emitters, γ emitters [7,8].

Polymeric microspheres: Types of polymeric microspheres can be categorized as follows and they are biodegradable polymeric microspheres and Synthetic polymeric microspheres.

Biodegradable polymeric microspheres: The natural polymers such as starch are used with the concept that they are biodegradable, biocompatible, and also bio adhesive in nature. These polymers will improve the residence time upon contact with mucous membrane due to its high degree of swelling property with aqueous medium, results gel formation. The rate and extent of drug release is associated by the concentration of polymer and the release pattern in a sustained manner. The major drawback is, in clinical use drug loading efficiency of biodegradable microspheres is complex and is difficult to analyze the drug release. However, they provide wide range of application in microsphere-based treatment [9].

Synthetic polymeric microspheres: In clinical application, the synthetic polymeric microsphere is widely used. They are also used as bulking agent, fillers, embolic particles, drug delivery vehicles etc. and proved to be effective and biocompatible. But the major drawback of these kind of microspheres, are they tend to migrate away from injection site and lead to, embolism and further organ damage.

Techniques Used in the Preparation of Microspheres

The choice of the technique mainly depends on the nature of the polymer used, the drug, the equivocally determined by some formulation and technology related factors as the requirement of the particle size, and the drug or the protein should not be adversely affected by the process, reproducibility of the release profile and the method and there should not be stability problem, and no toxic product(s) associated with the final product [10,11].

Different types of techniques that are employed for the preparation of the microspheres using hydrophobic and hydrophilic polymers as matrix materials are mentioned below.

1. Single emulsion technique
2. Double emulsion technique (Multiple emulsion)
3. Polymerization techniques
4. Phase separation coacervation technique
5. Spray drying
6. Non-aqueous solvent evaporation method
7. Ionic gelation method.

Methodology

Solvent evaporation method: Emulsification solvent evaporation involves the formation of an emulsion between polymer solution and an immiscible continuous phase whether aqueous (o/w) or non-aqueous.

The drug and polymeric solution is dispersed in a continuous phase containing emulsifying agent. It involves the use of a propeller type blade attached to a variable speed motor. Since high shear is used to produce the emulsion, the resultant product has a much smaller particle size than the emulsion produced by conventional agitation (Figure 1) [12].

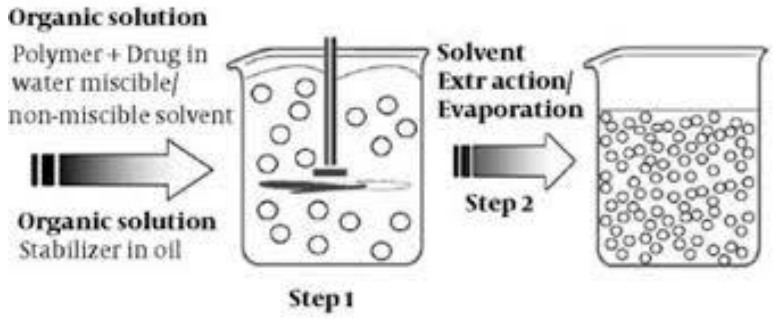

Figure 1: Schematic diagram showing solvent evaporation method.

Experimental methodology: Ethyl cellulose was weighed and dissolved in acetone to form a homogenous solution. Aspirin was accurately weighed and dissolved in polymeric solution. This solution was then added to 50 ml of aqueous phase containing 0.6% polyvinyl alcohol while being stirred at 800 rpm to emulsify the added dispersion as a fine droplet. The solvent removal was achieved by continuous stirring at room temperature for three hours to produce spherical microspheres. The microspheres formed were collected by filtration and washed repeatedly with distilled water. The product was then air dried [13].

Characterization and Evaluation

Study of drug excipient-interaction

There are several methods available to determine drug-excipient interaction.

The most commonly used processes, the obtained microspheres were evaluated for particle size, product yield, drug content, entrapment efficiency and loading capacity.

Determination of article size: Study of surface morphology of microsphere by scanning electron microscope (SEM).

The prepared amorphous nanoparticles were dispersed in deionized water and sonicated for 30 min. A circular metal plate is taken on to which carbon double tape (1 mm × 1 mm) is stickered; a drop of the resultant dispersion is placed on to the tape and allowed to dry for a while. Then it is scanned under SEM for morphology. The obtained microspheres were found to be spherical in shape (Figure 2).

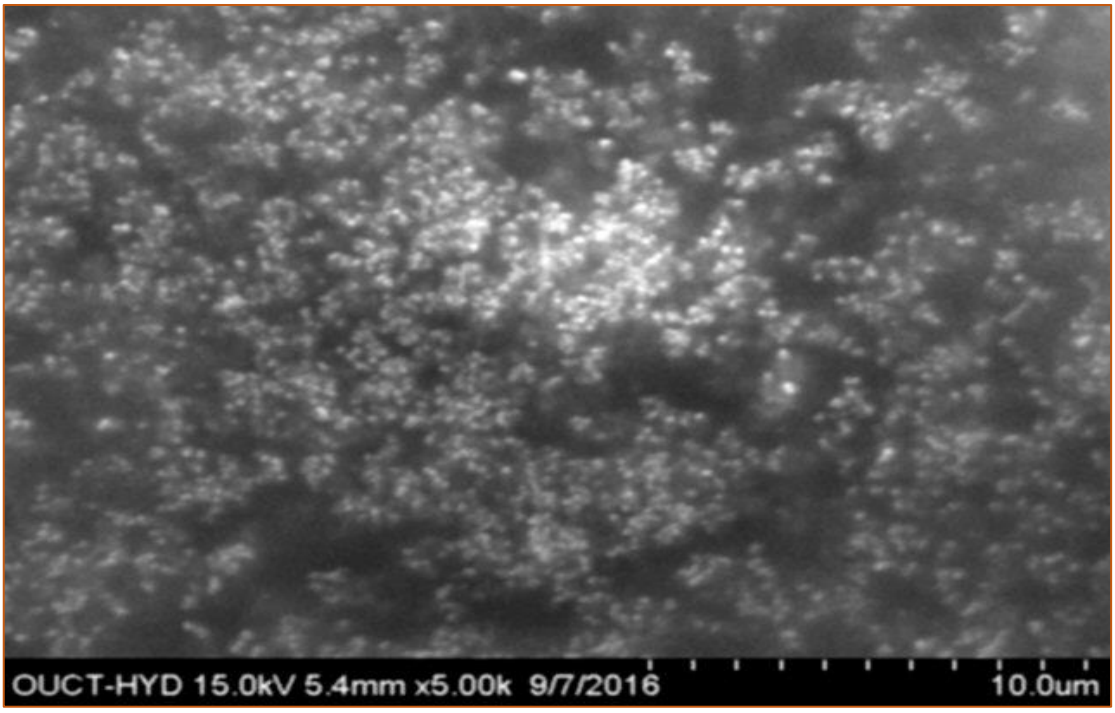

Figure 2: SEM image of aspirin loaded ethyl cellulose microspheres

Product yield: The yields of the prepared microspheres was calculated. The dried nanoparticles were weighed and the yield of nanoparticles was calculated using the formula:

$$Percentage\ yield = \frac{Amount\ of\ microparticles\ obtained}{Theoretical\ amount} \times 100$$

The product yield was observed as 90.6%

Drug content: To determine the drug content, 50 mg drug equivalent to formulation was weighed accurately and transferred into three necked RBF containing 50ml of methanol. The solution was stirred at 700 rpm for 3 hrs by using magnetic stirrer [8]. The resultant solution was filtered and the amount of the drug in the filtrate was estimated after suitable dilution by ultraviolet (UV) spectrophotometer. The drug content was found to be 80.3%.

Entrapment efficiency: Entrapment efficiency indicates the amount of drug encapsulated in the formulation. The method of choice for drug content determination is separation of free drug by ultracentrifugation, followed by quantitative analysis of the drug from the formulation. The samples were centrifuged by using ultracentrifuge at 17640 rpm for 40 min`[14].

Percentage entrapment efficiency may be calculated from the following formula:

$$Entrapment\ efficiency = \frac{Amount\ of\ drug\ encapsulated\ in\ the\ formulation}{Total\ amount\ of\ drug\ in\ the\ formulation} \times 100$$

The entrapment efficiency of the formulation was found to be 23.9%.

Loading Capacity: The loading capacity (L.C) refers to the percentage amount of drug entrapped in microspheres.

$$Loading\ capacity = \frac{Total\ amount\ of\ drug - Amount\ of\ unbound\ drug}{Nanoparticles\ weight} \times 100$$

The loading capacity was observed as 4.1%

Conclusion

Aspirin loaded ethyl cellulose microspheres were prepared by solvent evaporation technique. The obtained microspheres were evaluated for product yield, drug content, entrapment efficiency and loading capacity. The SEM images clearly reveals that the particles were found to be spherical in shape. The product yield, drug content, entrapment efficiency and loading capacity was found to be 90.6%, 85.3%, 23% and 4.1% respectively

References

1. Jain NK (2002) Controlled and novel drug delivery (4th Edn). New Delhi: CBS Publisher and Distributor, India 236-237.
2. https://en.wikipedia.org/wiki/Micro-encapsulation.
3. Simon B (1996) Microencapsulation methods and industrial application (2nd Edn). New York: Taylor & Francis.
4. Jackson LS, Lee K (1991) Microencapsulation and the food industry. Lebennsmittel- Wissenschaft Techonologie.
5. Thies C, Bissey MC (1983) Biomedical Applications of Microencapsulation. Florida: CRC Press, USA.
6. Kataria S, Middha A, Sandhu P, et al. (2011) Microsphere: A review. International Journal of Research in Pharmacy and Chemistry. 1(4): 1184-1198.
7. Bansal H, Kaur SP, Gupta AK (2011) Microsphere: Methods of preparation and applications; A comparative study. International Journal of Pharmaceutical Sciences Review and Research 10(1): 69-78.
8. Prasanth VV, Chakraborty Moy A, Mathew S, et al. (2011) Microspheres- An overview. International Journal of Research in Pharmaceutical and Biomedical Science 2(2): 332-338.
9. https://en.wikipedia.org/wiki/Microbeads.
10. Bhattarai RS, Dhandapani NV, Shrestha A (2011) Drug delivery using alginate and chitosan beads: An Overview. Chronicles of Young Scientists 2(4): 192-196.
11. Costas L, Pera LM, López AG, et al. (2012) Controlled Release of Sulfasalazine Release from 'Smart' Pectin Gel Microspheres under Physiological Simulated Fluids. Applied Biochemistry & Biotechnology 167(5): 1396.
12. Tavakol M, Vasheghani-Farahani E, Hashemi-Najafabadi S (2013) The effect of polymer and $CaCl_2$ concentrations on the sulfasalazine release from alginate-N, O-carboxymethyl chitosan beads. Progress in Biomaterials 2:10.
13. Rao TV, Vidhyadhara S (2012) Formulation and in vitro evaluation of indomethacin microcapsules. International Journal of Chemical Science 10(1): 1-8.
14. Tara C, Talsania M (2013) Formulation development and evaluation of microspheres containing duloxetine hydrochloride. International Journal of Research in Pharmaceutical and Biomedical Sciences 4(2): 568-572.