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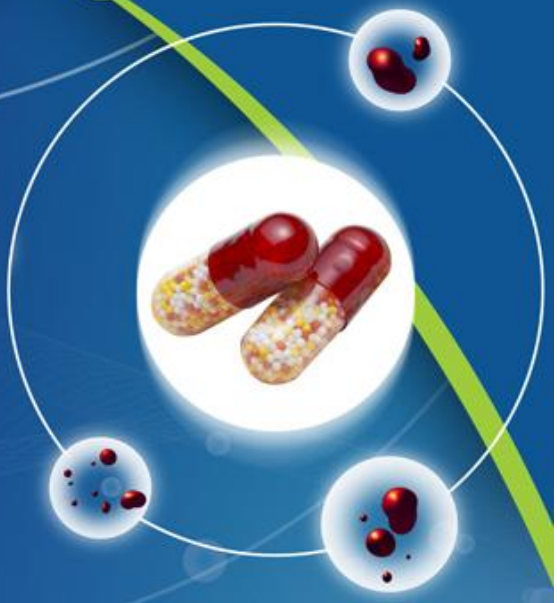

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Review Article

FLOATING MICROSPHERES AS NOVEL DRUG DELIVERY SYSTEM FOR ARTHRITIS

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ABSTRACT

The aim of this review work is to investigate the efficacy of floating microspheres as novel drug delivery system in arthritis. Drug delivery is defined as the process of administering the drug or pharmaceutical product to achieve desired therapeutic effect. Drug delivery has a significant effect on therapeutic efficacy. Novel drug delivery system has a major advance to solve the problems related to the drug release at specific site. There are various approaches for delivering the drug to the site. One such approach of novel drug delivery system is floating microspheres. The slow efficacy in the treatment of rheumatoid arthritis and osteoarthritis has suggested the growing need of floating microspheres as novel drug delivery system in arthritis. Rheumatoid arthritis is a chronic autoimmune disease characterized by inflammation of the lining or synovium. Rheumatoid arthritis affect 1% of the adult Indian population. Osteoarthritis is a common degenerative disorder of the articular cartilage along with hypertrophic bone changes. Risk factors of osteoarthritis are past trauma, genetics, obesity, and advancing age .All possible areas of floating microspheres is enlighted in this review work. Floating microspheres are in strict sense, spherical empty particles without core, free flowing powders consisting of proteins or synthetic polymers with a size in the range 1-1000 micrometer. This review work gives brief information about rheumatoid arthritis, osteoarthritis, floating microspheres, method of preparations and application of floating microspheres in drug delivery.

***Key words**: Floating microspheres, novel drug delivery system, osteorthritis, rheumatoid arthritis*

INTRODUCTION

A recent advance in novel drug delivery system is vital research areas which aim to enhance the safety and efficacy of the drug molecule. The aim of novel drug delivery system is to achieve a programmed delivery of the therapeutic substances to achieve maximum benefit [1]. The ability of drug loaded system to target to the site of interest is known as targeting [2]. From novel drug delivery systems new ideas emerged such as control of pharmacokinectics, pharmacodynamics, non- specific toxicity, immunogenicity, biorecognition and efficacy of drugs.

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These drug delivery systems are based on interdisciplinary approaches that include polymer science, pharmaceutics, bioconjugate and molecular biology. Various drug delivery system and drug targeting systems are currently under development with a goal on promoting the therapeutic effect of a drug and minimizing toxic effect. The very slow progress in the efficacy of the treatment of severe diseases such as arthritis has suggested a growing need of novel drug delivery system [3].

Indian researches have shifted their interest towards novel drug delivery system since early eighties as NDDS has several advantages over the conventional dosage forms. Novel drug delivery systems contribute a sizeable portion of the global market due to clinical advantages of the systems and their economic aspects. Relatively lesser investment of time and

money in novel drug delivery system could lead to higher margins of profit [4]. The inflammatory diseases such as rheumatoid arthritis (RA) and osteoarthritis experience limited treatment success with conventional therapy so now focussed on novel drug delivery systems. Arthritis results in a shortened life span. The past few years lead to a change in the approach to the treatment of arthritis. Arthritis are mainly rheumatoid arthritis and osteoarthritis[5].

RHEUMATOID ARTHRITIS

Rheumatoid arthritis is a chronic autoimmune disease characterized by inflammation of the lining or synovium. Rheumatoid arthritis affect 1% of the adult Indian population. (fig 1)

Pathopysiology of rheumatoid arthritis[6]

In rheumatoid arthritis the immune response will activated in an early stages triggered by genectic and environmental factors. Due to activation of T cells from an antigen presenting cell, subclinical inflammation occur ,once the immune system is unbalanced. The cascade of events occur in the immune system such as activation of B cells ad macrophages and proinflammatory mediators such as tumor necrosis factor(TNF) and interleukin(IL). After the diagnosis is confirmed, the pathologic inflammatory responses continue resulting in joint destruction as well as extra-articular complications. The bone and cartilage erosion will occur resulting in swollen joint capsule. The extra articular complications can occur which include infections, lymphomas, cardiovascular disease and osteoporosis.

Diagnosis of rheumatoid arthritis [7]

Due to the absence of signs and symptoms rheumatoid arthritis can be difficult to diagnose in its early stage. There is no blood test or physical finding to confirm diagnosis. There will be an elevated ESR in people with rheumatoid arthritis that indicate presence of anti inflammatory process in the body. Rheumatoid factor and anticyclic- citrullinate d peptide (anti-ccp) antibodies are mainly looked for blood test. X Rays help to track the progression of rheumatoid arthritis in joints over time.

Signs and symptoms of rheumatoid arthritis [8]

The signs and symptoms of rheumatoid arthritis can be mimicked by other diseases**.**

The 12 **signs** and symptoms of rheumatoid arthritis are the following

- Fatigue
- Joint pain
- Joint swelling
- Joint redness
- Joint warmth
- Joint stiffness
- Loss of joint range of motion
- Many joints affected (polyarthritis)
- Limping
- Joint deformity
- Both sides of the body affected (symmetric)

OSTEOARTHRITIS

osteoarthritis is a common degenerative disorder of the articular cartilage along with hypertrophic bone changes. Risk factors of osteoarthritis are past trauma, genetics, obesity, and advancing age.(fig 2)

Pathophysiology of osteoarthritis[9]

Osteoarthritis cause gross cartilage loss and morphological damage to other joint tissues. During onset of osteoarthritis the collagen matrix becomes more disorganized. The proteoglycan content within cartilage is decreased. The breakdown of collagen fibres results in increase in the water content. Inflammation of the synovium and the surrounding joint capsule can occur in osteoarthritis. The fibrotic and the menisci become damaged and ligaments within the joint become thickened. Osteophytes (new bone outgrowths, spurs) form on the margins of the joints. The pain in an osteoarthritic joint has been related to thickened synovium and subchondral bone lesions.

Diagnosis of osteoarthritis [10]

The main symptom of osteoarthritis is joint pain which tends to worsen with activity. Patients may report joint lockng or joint instability as well as morning stiffness. Patients limit their activities of daily living because of pain and stiffness. Physical examination is important in making the diagnosis as the joints are commonly affected such as hands, kness, hips and spine. Almost any joint can be involved.

Signs and symptoms of osteoarthritis [11]

Pain: Joint may hurt during or after movement.

Bone Spurs: These may be formed around the affected joint which feel like hard lumps.

Tenderness: When light pressure is applied to joint, it may feel tender.

Stiffness: Joint stiffness noticed when wake up in morning or after a period of inactivity.

Loss of Flexibility: Not able to move your joint through its full range of motion

Grating Sensation: Grating sensation when the joint is used.

The inflammation, join pain and stiffness associated with rheumatoid arthritis and osteoarthritis can be treated by Non Steroidal Anti inflammatory Drugs .NSAIDS (Non Steroidal Anti inflammatory Drugs) represent an inevitable place in the treatment of arthritis[12].

MECHANISM OF NSAIDS (NON STEROIDAL ANTI INFLAMMATORY DRUGS)

NSAIDS work to decrease inflammation, pain and fever. NSAIDS block enzymes that help in the production of prostaglandins. Prostaglandins play a role in pain and inflammation which is a group of naturally occurring fatty acids.

Effective drug delivery of NSAIDS can be done by novel drug delivery system such as floating microspheres.

FLOATING MICROSPHERES [13]

Floating microspheres are gastro retentive drug delivery systems based on non effervescent approach. Floating microspheres enhance the bioavailability of drugs. Floating microspheres are in strict sense, spherical empty particles without core, free flowing powders consisting of proteins or synthetic polymers with a size in the range 1-1000 micrometer. Floating microspheres will remain buoyant over gastric contents for a prolonged period of time. Hollow microspheres can be prepared by emulsion solvent diffusion method. For example hollow microballoons loaded with ibuprofen in their outer polymer shells was prepared by emulsion-solvent diffusion method. The ethanol, dichloromethane solution of the drug as well as enteric acrylic polymer was poured in to an agitated aqueous solution of polyvinyl alcohol which was thermally controlled at 40^0c. By evaporation of dichloromethane the gas phase was generated in dispersed polymer droplets. The microballoons floated continuously over the surface of acidic dissolution for greater than 12 hours by in vitro method .

Advantages of floating microspheres

- Improve patient compliance by decreasing dosing frequency
- Better therapeutic effect
- Gastric retention time is increased because of buoyancy
- Release of drug for a prolonged period in a controlled manner
- Site specific drug delivery
- Superior to single unit floating dosage systems such as microspheres

Disadvantages of floating microspheres [14]

- Floating drug delivery system requires presence of food to delay their gastric emptying
- High variability in gastric emptying due to its all or non emptying process
- Patients should not be dosed with floating forms before going to bed

Mechanism of floating microspheres

The colloidal gel barrier forms as the microspheres come in contact with gastric fluids due to the gel formers, polysaccharides and due to hydration of polymers. This colloidal gel barrier controls the rate of fluid penetration into the device and consequent drug release. The gel layer is maintained by the hydration of adjacent hydrocolloidal layer as the exterior surface. The air trapped confers buoyancy to the microspheres. Some of the recent developments are hollow microspheres of acrylic resins, eudragit, polyethylene oxide cellulose acetate, polystyrene floatable shells, polycarbonate floating balloons..

Methods for the preparation of floating microspheres [15]

Various methods are used for the preparation of hollow microspheres such as solvent evaporation, emulsion solvent diffusion, spray drying and miscellaneous methods.

- ***Solvent Evaporation Method***
  In this method the drug and the polymer are dissolved in an organic phase and dispersed in an excess amount of aqueous continuous phase with the help of magnetic stirrer which results in an emulsion. For insoluble or poorly water- soluble drugs, the oil in water method is used but for hydrophilic

drugs this method is inappropriate due to dissolution and extensive loss of drug.

- ***Emulsion solvent diffusion method***

This method involves mixing of drug and solution of polymer in dichloromethane and ethanol into an agitated aqueous solution of surfactants. Into the external phase the ethanol rapidly partitions and polymer precipitates around dichloromethane droplets. The evaporation of entrapped dichloromethane leads to the formation of internal cavities within the microspheres.

- ***Spray drying***

Spray drying is the most widely employed industrial process used for particle formation as well as drying. It a single step ideal process where the required particle size distribution, bulk density and particle size can be obtained.

- ***Miscellaneous***

The various miscellaneous methods are used for the preparation of floating microspheres. Example of hollow microspheres prepared by miscellaneous method is hollow microspheres as a device for controlled delivery of proteins.

Applications of floating microspheres [16]

- Floating microsphere is used in delivery of sparingly soluble and insoluble drugs.
- The gastro retentive floating microspheres enhance bioavailability of drugs by altering the absorption profile of active agent.
- Drugs that have poor bioavailabiity can be delivered by maximizing their absorption and improving the bioavailability.
- Floating microspheres are used for the treatment of gastric and duodenal cancers.
- Hollow microspheres used to treat stomach and duodenal ulcers, gastritis and oesophagitis.

CONCLUSION [17]

As the floating dosage forms provide definite advantages, it is a better choice for drug delivery in arthritis. The current advancements in novel drug delivery systems are helpful in overcoming challenges offered by the traditional systems. It also provide solutions to enormous questions that were remained unanswered.

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REFERENCES

1. *U. Ramchandani, S.K Shrivastava, P.K Dubey. Current trends in NDDS with special reference to NSAIDS. Int J Pharma and Biosci 2011;2 (1): 92-114*
2. *Arun R, Novel Drug Delivery System. Available from (11 Jan 2016)*
3. *Manivannan R, Kugalur G,Parthiban. Recent Advances in Novel Drug Delivery System. Int J Res Ayur and Pharma 2010;1(2): 316-26.*
4. *Dr Subhash C M, Dr Moitreyer M. Current Status and Future Prospects of New Drug Delivery System. Pharma Times 2010; 42(4): 13-6*
5. *R. Handa, Management of Rheumatoid Arthritis. Natl Med J India 2004; 17 (3): 143-51*
6. *Jennifer N C. Treatment of Rheumatoid Arthritis: A review of Recommendations and Emerging Therapy. Formulary J 2011; 46: 532-45.*
7. *www. Mayoclinic.org/diseases-conditions/rheumatoid-arthritis/basics/tests-diagnosis/con-20014868(8 Jan 2016)*
8. *www.medicinenet.com/rheumatoid arthritis early symptoms /article. htm (9 Jan 2016)*
9. *https://en.wikipedia.org/wiki/osteoarthritis#pathophysiology. (9 Jan 2016)*
10. *Keith S MD. Osteoarthritis :Diagnosis and Treatment. Am Fam Physician 2012; 85(1): 49-56.*
11. *www.mayoclinic.org/disease-conditions/osteo arthritis/basics/symptoms/con-20014749(9 Jan 2016)*
12. *Kapil K. A.K Rai. Evaluation of Antiinflammatory and Antiarthritic Activities of Floating Microspheres of Herbal Drug. Int Res J Pharma 2012; 3(1): 186-93.*
13. *Rajkumar K, Sainath G R, Sai S P, Anusha P, Lavanya A S, E.R Reddy. Floating Microspheres a novel approach in drug delivery. J Drug Delivery Res 2012; 1(4):1-20*
14. *Vishal B, Nirmala S L, Harikumar . Floating Drug Delivery System. Pharmacophore 2013; 4 (1): 26-38 .*
15. *Kurrey. Hollow microspheres as a drug carrier: An overview of fabrication and in vivo characterization technique. Downloaded free from*

http://www.cysonline.org on Friday. 8 Jan,2016,IP: 117.211.166.126.

16. *P Dutta, J Sruti, Ch Niranjan P, M .E Bhanoji Rao. Floating microspheres Recent trends in the development of gastroretentive FDDS. Int J of Pharma Sci and Nanotech 2011; 4(1):1296-306*
17. *Manish K S, Rajesh A, Avinash G,Deepak S. Floating microsphere Recent Research. Gratis J Pharma and Therap 2015; 1(1): 11-8.*