INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH AND BIOMEDICAL ANALYSIS | ISSN: 2278 –2664
| JAN-MAR 2014| VOLUME 3 | ISSUE 1 | 01-06
Available Online Through: www.ijprba.com

Research Article

NANOSPONGES -A CONCISE REVIEW FOR EMERGING TRENDS

Susmitha Bezawada[1]*, Charanjitha[2], V.Manisha Reddy[3], Naveena[4], V.Ram Mohan Gupta[5]

Pulla reddy institute of pharmacy, Dundigal, Annaram (v), 502 313.

***Corresponding author E-mail: susmithabezawada@gmail.com**

ABSTRACT

The advent of nanotechnology lead to invention of many dosage forms. Effective targeted drug delivery systems have been a dream for a long time, due to several major drawbacks, a practical approach has been developed for the formation of discrete functionalized particles, which have been termed as 'nanosponges'. These tiny sponges can circulate around the body until they encounter the specific target site and stick on the surface and begin to release the drug in a controlled and predictable manner. Owing to their small size and porous nature they can bind poorly-soluble drugs within their matrix and improve their bioavailability. They can be crafted for targeting drugs to specific site, prevent drug and protein degradation .This review attempts to elaborate the interesting features of nanosponges, preparation, Characterization, applications and recent updates of nanosponges in drug delivery.

KEY WORDS

nanosponges, nanotechnology, synthesis, preparation.

INTRODUCTION

Effective targeted drug delivery systems have been a dream for long time, but it has been largely frustrated by the complex chemistry that is involved in the development of the new systems. The invention of the nanosponges has become a significant step towards overcoming these problems. Nanosponges were originally developed for topical delivery of drugs. Nanosponges are tiny sponges with a size of a virus with an average diameter below 1µm.These tiny sponges can circulate around the body until they encounter the specific target site and stick on the surface and began to release the drug in a controlled and predictable manner. Because the drug can be released at the specific target site instead of circulating throughout the body it will be more effective for a particular given dosage. Nanosponges are capable of providing solutions for several formulation related problems. Owing to their small size and porous nature they can bind poorly- soluble drugs within the matrix and improve their bioavailability. They can be crafted for targeting drugs to specific sites, prevent drug and protein degradation and prolong drug release in a controlled manner. Nanosponges are obtained by suitable cross linking process and also by different organic and inorganic materials. Nanosponges can encapsulate

various types of molecules by forming inclusion and non inclusion complexes.

Features of nanosponges

An important character of these sponges is their aqueous solubility; this allows the use of these systems effectively for drugs with poor solubility.

The Nanosponges are capable of carrying both lipophilic and hydrophilic drugs.

They have been used for removal of organic impurities in water, as nano-carriers for biomedical applications.

This technology offers entrapment of ingredients and reduced side effects, improved stability, increased elegance, and enhanced formulation flexibility. Nanosponges are non irritating and non-mutagenic, non-allergic and nontoxic. Extended release-continuous release up to 12h allows incorporation of immiscible liquid improves material processing-liquid can be converted to powders. They can be formed in a sub microns spherical particle. They can be obtained in a wide range of dimensions, from 1micron to 10microns. The cavities of the framework have a tunable polarity.

Different functional groups can be linked to the structure due to sub micron dimensions of the particle. Nanosponges can disperse at molecular level, highly insoluble principles, stabilizing and protecting their structures, from chemicals, light, oxygen, etc. efficacy and shelf life of drugs can be prolonged if compared to the non-complexed form. By using Nanosponges as drug delivery system, higher therapeutic activities are observed being the concentration of the active molecule the same.

SYNTHESIS OF NANOSPONGES

Solvent method

Mix the polymer with a suitable solvent, in particular in a polar aprotic solvent such as Dimethylformamide,dimethylsulfoxide. Then add this mixture to excess quantity of the cross-linker, preferably in cross linker/polymer molar ratio of 4to 16. Carry out the reaction at temperature ranging from 10°C to the reflux temperature of the solvent, for time ranging from 1 to 48h. Preferred crosslinkers are carbonyl compounds (Dimethyl carbonate & Carbonyldiimidazole) After completion of the reaction, allow the solution to cool at room temperature, then add the product to large excess of distilled water and recover the product by filtration under vacuum and subsequently purify by prolonged sox let extraction with ethanol. Dry the product under vacuum and grind in a mechanical mill to obtain homogeneous powder.

Ultrasound-Assisted synthesis

In this method nanosponges can be obtained by reacting polymers with cross-linkers in the absence of solvent and under sonication. The nanosponges obtained by this method will be spherical and uniform in size .Mix the polymer and the cross-linker in a

Particular molar ratio in a flask. Place the flask in an ultrasound bath filled with water and heat it to 90°C. Sonicate the mixture for 5hours. Then allow the mixture to cool and break the product roughly.Wash the product with water to remove the non-reacted polymer and subsequently purify by prolonged sox let extraction with ethanol. Dry the obtained product under vacuum and store at 25°C until further use

Loading of drug into nanosponges

Nanosponges for drug delivery should be pretreated to obtain a mean particle size below

500nm.Suspend the nanosponges in water and sonicate to avoid the presence of aggregates and then centrifuge the suspension to obtain the colloidal fraction. Separate the supernatant and dry the sample by freeze drying. Prepare the aqueous suspension of Nanosponges disperse the excess amount of the drug and maintain the suspension under constant stirring for specific time required for complexation. After complexation, separate the uncomplexed (undissolved) drug from complexed drug by centrifugation. Then obtain the solid crystals of nanosponges by solvent evaporation or by freeze drying

Crystal structure of nanosponges plays a very important role in complexation with drug. A study revealed that paracrystalline nanosponges showed different loading capacities when compared to crystalline nanosponges. The drug loading is greater in crystalline nanosponges than paracrystalline one. In poorly crystalline nanosponges, the drug loading occurs as a mechanical mixture rather than inclusion complex.

Type of drugs

Drug molecules to be complexed with nanosponges should have certain characteristics mentioned below

- Molecular weight between 100 and 400
- Drug molecule consists of less than five condensed rings
- Solubility in water is less than 10mg/mL
- Melting point of the substance is below 250°C

CHARACTERIZATION OF NANOSPONGES

Inclusion complexes formed between the drug and nanosponges can be characterized by following methods.

Thermo-analytical methods

Thermo-analytical methods determine whether the drug substance undergoes some change before the thermal degradation of the nanosponges. The change of the drug substance may be melting, evaporation, decomposition, oxidation or polymorphic transition. The change of the drug substance indicates the complex formation. The thermo gram obtained by DTA and DSC can be observed for broadening, shifting and appearance of new peaks or disappearance of certain peaks. Changes in the weight loss also

can provide supporting evidence for the formation of inclusion complexes.

Microscopy studies

Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) can be used to study the microscopic aspects of the drug, nanosponges and the product (drug/nanosponge complex). The difference in crystallization state of the raw materials and the product seen under electron microscope indicates the formation of the inclusion complexes.

X-ray diffractiometry and single crystal X-ray

Structure analysis

Powder X-ray diffractiometry can be used to detect inclusion complexation in the solid state. When the drug molecule is liquid since liquid have no diffraction pattern of their own, then the diffraction pattern of a newly formed substance clearly differs from that of uncomplexed nanosponge. This difference of diffraction pattern indicates the complex formation. When the drug compound is a solid substance, a comparison has to be made between the diffractogram of the assumed complex and that of the mechanical mixture of the drug and polymer molecules .A diffraction pattern of a physical mixture is often the sum of those of each component, while the diffraction pattern of complexes are apparently different from each constituent and lead to a "new" solid phase with different diffractograms. Diffraction peaks for a mixture of compounds are useful in determining the chemical decomposition and complex formation.The complex formation of drug with nanosponges alters the diffraction patterns and also changes the crystalline nature of the drug. The complex formation leads to the sharpening of the existing peaks, appearance of a few new peaks and shifting of certain peaks.

Single crystal X-ray structure analysis may be used to determine the detailed inclusion structure and mode of interaction. The interaction between the host and guest molecules can be identified and the precise geometrical relationship can be established

Solubility studies

The most widely used approach to study inclusion complexation is the phase solubility method described by Higuchi and Connors, which examines the effect of a nanosponge, on the solubility of drug. Phase solubility diagrams indicate the degree of complexation

Infra-Red spectroscopy

Infra-Red spectroscopy is used to estimate the interaction between nanosponges and the drug molecules in the solid state. Nanosponge bands often change only slightly
upon complex formation and if the fraction of the guest molecules encapsulated in the complex is less than 25%, bands which could be assigned to the included part of the guest molecules are easily masked by the bands of the spectrum of nanosponges. The technique is not generally suitable to detect the inclusion complexes and is less clarifying than other

methods .The application of the Infra-red spectroscopy is limited to the drugs having some characteristic bands, such as carbonyl or sulfonyl groups. Infrared spectral studies give information regarding the involvement of hydrogen in various functional groups. This generally shifts the absorbance bands to the lower frequency, increases the intensity and widens the band caused by stretching vibration of the group involved in the formation of the hydrogen bonds. Hydrogen bond at the hydroxyl group causes the largest shift of the stretching vibration band.

Thin Layer Chromatography

In Thin Layer Chromatography, the Rf values of a drug molecule diminishes to considerable extent and this helps in identifying the complex formation between the drug and nanosponge.

Loading efficiency

The loading efficiency of nanosponges can be determined by the quantitative estimation of drug loaded into nanosponges by UV spectrophotometer & HPLC methods.

Particle size and polydispersity

The particle size can be determined by dynamic light scattering using 90 Plus particle sizer equipped with MAS OPTION particle sizing software. From this the mean diameter and polydispersity index can be determined.

CONCLUSION

The nanosponges have the ability to include either lipophilic or hydrophilic drugs and release them in a controlled and predictable manner at the target site. By controlling the ratio of polymer to the cross-linker the particle size and release rate can be modulated. Nanosponges enable the insoluble drugs and protect the active moieties from physicochemical degradation and controlled release. Because of their small size and spherical shape nanosponges can be developed as different dosage forms like parenteral, aerosol, topical, tablets and capsules.

REFERENCES

1. Trotta F, Cavalli R, Tumiatti W, Zerbinati O,Rogero C, Vallero R. Ultrasound-assisted synthesis of Cyclodextrin-based nanosponges. EP1 786 841 B1; 2007.
2. David F. Nanosponge drug delivery system more effective than direct injection. www.physorg.com 01.06.2010, accessed on 20.12.2011.
3. Trotta F, Tumiatti V, Cavalli R, Rogero C,Mognetti B, Berta G. Cyclodextrin-based nanosponges as a vehicle for Antitumoral drugs.WO 2009/003656 A1; 2009.
4. Liang L, De-Pei L, Chih-Chuan L. optimizing the delivery systems of chimeric RNA. DNA oligonucleotides beyond general oligonucleotide transfer. Eur. J. Biochem. 2002; 269: 5753–5758.
5. Jenny A, Merima P, Alberto F, Francesco T. Role of β- cyclodextrin nanosponges in polypropylene photo-oxidation. Carbohydrate Polymers, 2011; 86:127– 135.
6. Leslie Z. Benet., BCS and BDDCS.Bioavailability and Bioequivalence: Focus on Physiological Factors and

Variability. Department of biopharmaceutical sciences, University of California, San Francisco, USA, 2007.

7. Renuka S, Roderick BW, Kamla P. Evaluation ofthe kinetics and mechanism of drug release from Econazole Nitrate nanosponge loaded carbapol hydrogel. Ind J Parm Edu Res, 2011; 45(1): 25-31.
8. Renuka S, Kamla P. Polymeric nanosponges as an alternative carrier for improved retention of econazole nitrate onto the skin through topical hydrogel formulation Pharm Dev Technol. 2011; 16(4):367-376.