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Design And Development Of Nanosponges For Topical Application

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Abstract: A Nanosponge is a size of virus with a scaffold structure of naturally degradable polyester. The long length polyester strands are mixed in solution with small molecules called cross-linkers that have an affinity for certain portions of the polyester. They 'cross link' segments of the polyester to form a spherical shape that has many pockets (or cavities) where drugs can be stored. The polyester is biodegradable i.e. breaks up in the body to release the drug on a known schedule. Nanosponges come under the class of encapsulating nanoparticles which encapsulate drug molecules within its core. These nanosponges represent a novel class of nanoparticles usually obtained by natural derivatives. As compared to the other nanoparticles, they are insoluble both in water and organic solvents, porous, nontoxic and stable at high temperatures up to 300°C. The Caspofungin nanosponges can be formulated by cost effective and easy emulsion solvent diffusion method using hydrophobic polymers such as eudragit. The formulated Caspofungin nanosponges can be used in the treatment of breast cancer. This can be targeted to the cancer cells and produce sustained drug delivery which in turn reduces the dose, frequency of administration and the side effects.

Index Terms - Nanosponge, degradable polyester, nanoparticles, eco-compatible, Caspofungin and emulsion solvent diffusion method.

I. INTRODUCTION

A Nanosponge is a size of virus with a scaffold structure of naturally degradable polyester. The long length polyester strands are mixed in solution with small molecules called cross-linkers that have an affinity for certain portions of the polyester. They 'cross link' segments of the polyester to form a spherical shape that has many pockets (or cavities) where drugs can be stored. The polyester is biodegradable i.e. breaks up in the body to release the drug on a known schedule. Nanosponges come under the class of encapsulating nanoparticles which encapsulate drug molecules within its core. These nanosponges represent a novel class of nanoparticles usually obtained by natural derivatives. As compared to the other nanoparticles, they are insoluble both in water and organic solvents, porous, nontoxic and stable at high temperatures up to 300°C. They have ability to capture, transport and selectively release a huge variety of substances because of their 3-dimensional structure containing cavities of nanometric size and tunable polarity. Furthermore, nanosponges show a remarkable advantage in comparison with the common nanoparticles: indeed, they can be easily regenerated by different treatments, such as washing with eco-compatible solvents, stripping with moderately inert hot gases, mild heating, or changing pH or ionic strength. For all these characteristics, nanosponges have been already employed in different applied fields, such as cosmetic and pharmaceutical sectors. (Bolisetti S, 2012).

2 Synthesis of nanosponges : (Vishwakarma A, 2014)

It is one of the important criteria for the formation of product obtained activity in β-cyclodextrin, titanium oxide.

2.1) Solvent method:

The solvent required will be mix with the polymer mainly in a polar aprotic solvent for exampledimethylforamide, dimethylsulfoxide then add this mixture to cross linker in a exceed quantity, the ratio for cross linker/ molar ratio is preferred as 4 to 16. The reaction is proceed with a solvent reflux temperature and time ranging from 1 to 48 hr(21). The cross linkers which may preffered are dimethyl carbonate and carbonyl diimidazole. The reaction is completed and solution is allow to cool at room temperature then product is added to excess of bi-distilled water and product is recovered by filtration under vaccum and simultaneously purify by prolonged soxhlet extraction with ethanol. Finally product is dried under vaccum and grinded in a mechanical mill to obtain homogeneous powder.

2.2) Ultrasound assisted synthesis:

Nanosponges are obtained by reacting polymer with cross linkers without adding or without using solvent and sonification is maintained. The size obtained by this technique wil be spherical and uniform. The polymer is mix with a cross linkers in a balanced ratio in a flask. The flask is placed in a molar ratio in an ultrasound bath field with water and temperature maintained at 90ºc. the mixture is sonicated for 5hr. Then the mixture is kept to cool and product is break roughly then the product is washed with water to remove non-reacted polymer and subsequently purified by soxhlet extraction with ethanol. The product is dried under vaccum at 25ºc until its further use is utilized.

2.3) Loading of drug into nanosponges:

Nanosponges obtained should be pretreated to maintain mean particle size blow 500nm. Nanosponges are suspended in water and were sonicated to avoid presence of aggregates and particles and got centrifuged to obtain colloidal fraction, then supernatant is separated and dried sample by freezing by drying. Further proceeding start with preparing aqueous suspension of nanosponges and excess amount of drug is dispensed for maintaining suspension under constant stirring for specific time period for complexation is over the undissolved drug (uncomplexed condition) is separated from complexed drug with the process of centrifugation. This process helps in evolving solid crystals of nanosponges by solvent evaporation or freeze drying. Nanosponges crystal play important part in complexation with drug. Para-crystalline nanosponges revealed different loading capacities when compared to crystalline nanosponges poorly crystalline nanosponges had act drug loading as a mechanical mixture rather than inclusion complex.

3 FORMULATIONS OF CASPOFUNGIN NANOSPONGES BY EMULSION SOLVENT DIFFUSION METHOD:

Emulsion solvent diffusion method was used to formulate Caspofungin loaded nanosponges by using a suitable polymer. Dispersed phase consist of specified amount of drug and polymer which was dissolved in 20 ml of an organic solvent dichloromethane. Aqueous phase consist of specified amount of poly vinyl alcohol dissolved in 100 ml distilled water. Disperse phase was added drop by drop into aqueous phase by stirring on magnetic stirrer at 1000 rpm for about 2 hours. The nanosponges formed were collected by filtration and dried in oven at 40°c for about 24 hours. They were then kept in the vacuum desiccators to remove the residual solvent. The Caspofungin nanosponges were formulated using polymers ethyl cellulose and eudragit.

4. EXCIPIENTS COMPATIBILITY STUDIES

Fourier Transform Infrared (FT-IR) spectra of the samples were obtained using a SHIMADZU Spectrometer by KBr disc method. The spectrums were recorded for the pure drug and physical mixture of drug and polymer and are shown in Figures 1, 2 and 3.

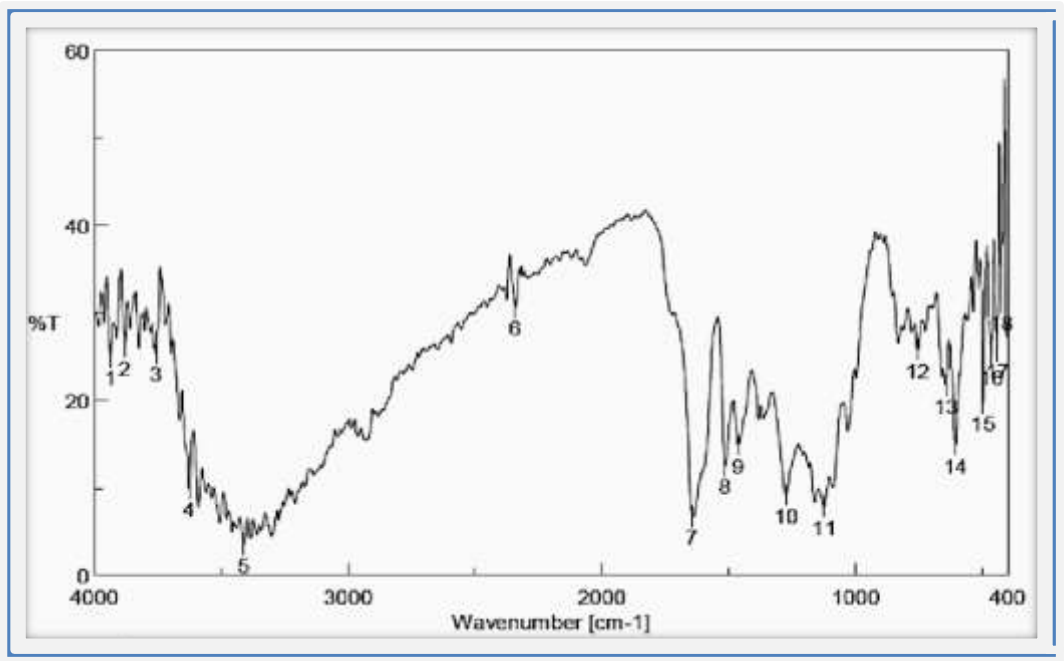

Figure 1: FTIR – spectrum of Caspofungin

Table 1: FTIR interpretation of Caspofungin

Materials	**Standard wave number (cm^{-1})**	**Test wave number (cm^{-1})**	**Functional group assignment**
Caspofungin	3650-3200	3410.49 3625.52	OH stretching
	1820-1665	1643.05	C=O stretching
	1320-1210	1273.75	C-O-C stretching
	1161-1029	1121.4	In plane =C-H bending

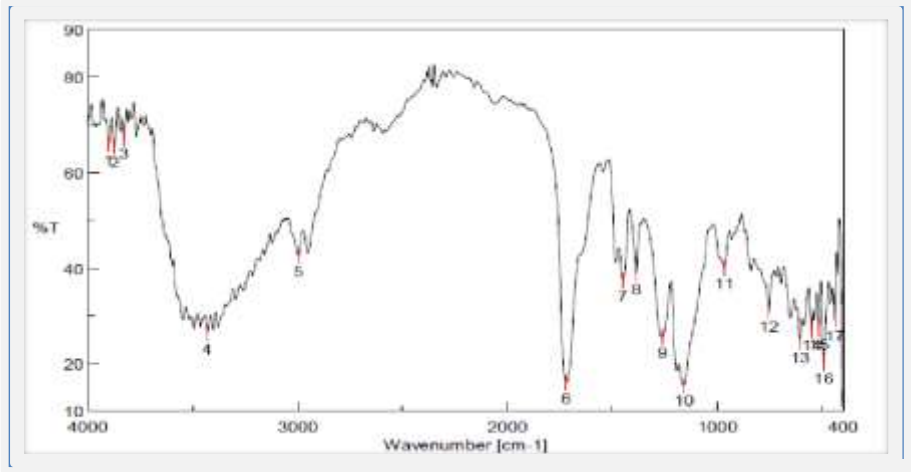

Figure 2: FTIR spectrum of Eudragit

Table 2: FTIR interpretation of Eudragit

Materials	Standard wave number(cm^{-1})	Test wave number (cm^{-1})	Functional group assignment
EUDRAGIT	3000-3700	3430.74	O-H stretching
	1500-1800	1720.19	N-H bending
	2700-3300	2995.87	C-H stretching
	1300-1500	1451.17 1386.57	C-H bending
	1000-1300	1262.18 1159.01	C-O stretching

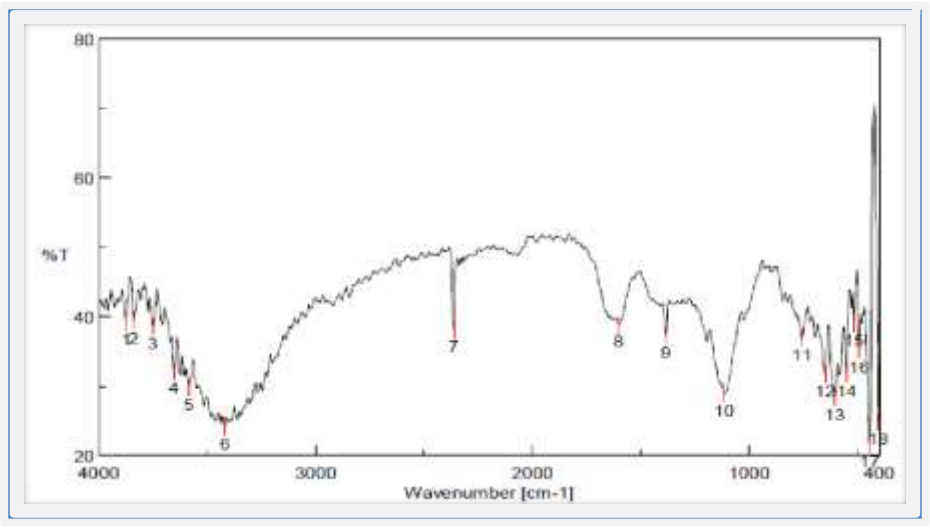

Figure 3: FTIR spectrum of Poly Vinyl Alcohol (PVA)

Table 3: FTIR interpretation of Poly Vinyl Alcohol

Materials	Standard wave number(cm^{-1})	Test wave number(cm^{-1})	Functional group assignment
POLYVINYL ALCOHOL	3300-3600	3584.06	OH stretching
	2850-2970	2862.37	CH_3 stretching
	1500-1760	1600.63	COOH
	1340-1470	1383.68	Alkanes bending
	1000-1300	1116.58	C-O stretching
	600-800	757.888 648.929	C-H rocking

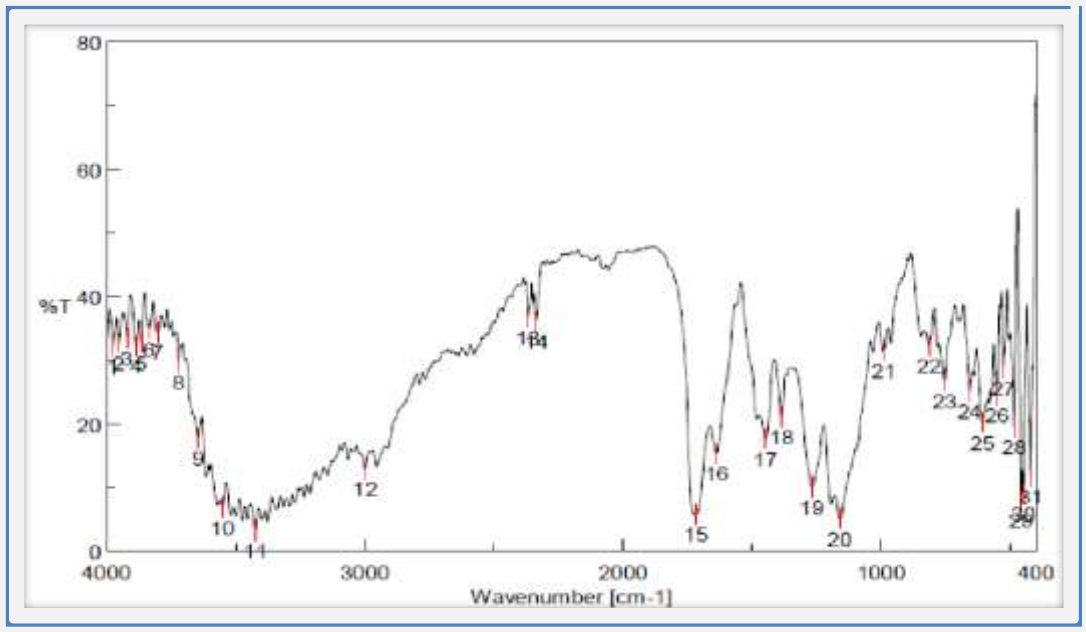

Figure 4:FTIR spectrum of physical mixture containing Caspofungin, Eudragit and PVA

Table 4: FTIR interpretation of mixture containing Caspofungin, Eudragit and PVA

Materials	Standard wave number (cm^{-1})	Test wave number (cm^{-1})	Functional group assignment
MIXTURE CONTAINING CASPOFUNGIN,	3650-3200	3642.87 3423.033	OH stretching
	3300-2700	2999.73	C-H stretching
	1820-1665	1718.26	C=O stretching
	1800-1500	1639.2	N-H bending
	1500-1300	1386.57	C-H bending

EUDRAGIT and PVA	1320-1210	1268.93	C-O-C stretching
	1161-1029	1161.9	In plane =C-H bending
	800-600	814.777 658.571	C-H rocking

The peaks present in the FTIR spectra of pure Caspofungin are present in the FTIR spectra of physical mixture containing Caspofungin with ethyl cellulose and Caspofungin with eudragit. It is therefore evident that the Caspofungin is compatible with the excipients ethyl cellulose eudragit and poly vinyl alcohol and can be chosen for the formulation of Caspofungin nanosponges.

5. FORMULATION OF NANOSPONGES

Selection of polymers for the formulation of Caspofungin nanosponges by emulsion solvent diffusion method was based on the trial batches carried out by using different polymers such as ethyl cellulose, eudragit, sodium alginate, HPMC, Carbopol, hydroxyl ethyl cellulose, chitosan and pectin and details are depicted in table 5. Drug: polymer ratio was selected based on the literature. The results indicated that ethyl cellulose and eudragit was found to be suitable for the formulation of Caspofungin nanosponges.

Table 5: Trial batches for formulation of Caspofungin nanosponge

Drug	Polymer	Ratio	Result observed
CASPOFUNGIN	Ethyl cellulose	1:2	Product obtained
	Eudragit	1:2	Product obtained
	Hydroxy propyl methyl cellulose	1:2	Less yield
	Hydroxyl ethyl cellulose	1:2	Less yield
	Carbopol	1:2	Gel like product
	Sodium alginate	1:2	Gel like product
	Chitosan	1:2	No product
	Cyclodextrin	1:2	No product
	Pectin	1:2	No yield

Total ten formulations (F1 – F5 and F6 – F10) of Caspofungin nanosponges with two different polymers ethyl cellulose and eudragit in different ratios were formulated by emulsion solvent diffusion method as given in Table 6 and Table 7.

Table 6: Formulation of Caspofungin nanosponges

S. No	Formulation code	Drug	Polymer	Drug: polymer Ratio
1	F1	CASPOFUNGIN	Ethyl cellulose	1:0.5
2	F2		Ethyl cellulose	1:1
3	F3		Ethyl cellulose	1:1.5
4	F4		Ethyl cellulose	1:2
5	F5		Ethyl cellulose	1:3
6	F6		Eudragit	1:0.5
7	F7		Eudragit	1:1
8	F8		Eudragit	1:1.5
9	F9		Eudragit	1:2
10	F10		Eudragit	1:2.5

Table 7: Formulation of Caspofungin nanosponges by emulsion solvent diffusion technique

S. No	Formulation code	Weight of drug (mg)	Weight of polymer (mg)	Weight of polyvinyl alcohol(mg)
1	F1	100	50	200
2	F2	100	100	200
3	F3	100	150	200
4	F4	100	200	200
5	F5	100	300	200
6	F6	100	50	200
7	F7	100	100	200
8	F8	100	150	200
9	F9	100	200	200
10	F10	100	250	200

5.2 Scanning Electron Microscopy

SEM analyses of the formulated Caspofungin nanosponges were performed to evaluate the surface morphology of nanosponges. The SEM images of formulation F9 are shown in Figure 5
SEM images showed the nanosponge was porous with a smooth surface morphology and spherical in shape. The spongy and porous nature of the nanosponges can be seen in the above figures.The presence of pores was due to the impression of diffusion of the solvent dichloromethane.

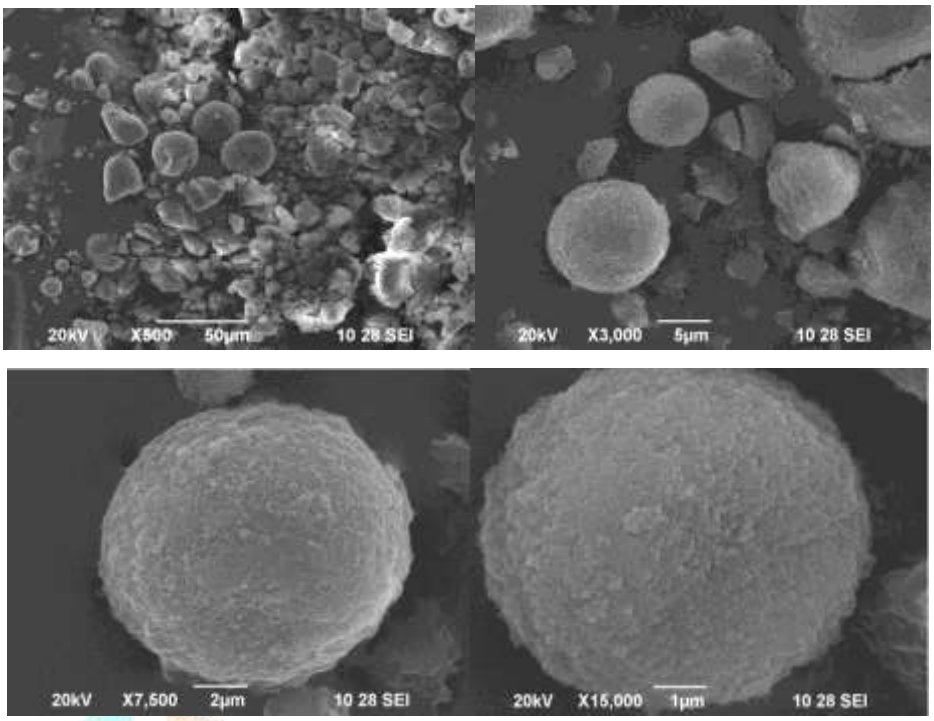

Figure 5: SEM images of Caspofungin nanosponges using eudragit

REFERENCES

[1] Bolisetti SS, Indira B, Samrat CH and Reddy SM, 2012, Nanosponges: A New Era in Drug Delivery : Review, Journal of Pharmacy Research, 5(12),5293-5296.

[2] Vishwakarma A, Nikam P, Mogal R and Talele S, 2014, Review On Nanosponges: A Benefication for Novel Drug Delivery, International Journal of PharmTech Research, 06(1):11-20

[3] Preethi S, Ananya KV, Patil AB and Gowda DV 2020, Recent review on Nano sponge, International Journal of Research in Pharmaceutical Sciences. Vol.11(1), 1085-1096.

[4] Jeganath S, Nitish, Khilifa Fathelrahman Khalifa Abdelmagid, A Review on Nanosponges – A Promising Novel Drug Delivery System, Research J. Pharm. and Tech, 2021; 14(1):501-505.

[5] MurlidharTarge B., Patil M.P., Jahagirdar A.C., Khandekar B.D., "Nanosponges – An Emerging Drug Delivery System". Int J Inst Pharm Life Sci. November-December 2015;

[6] Padmini I, N. Vishal Gupta & Riyaz Ali M. Osmani & V. Balamuralidhara, "Design & development of nanosponge loaded topical gel of curcumin and caffeine mixture for augmented treatment of psoriasis", DARU Journal of Pharmaceutical Sciences, 2020, 28:489–506