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Original Article

Enhancement of Solubility of Albendazole by Inclusion Complexation with Nanosponges and β-Cyclodextrin

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ABSTRACT

Aim: Objective of work was to compare role of β-Cyclodextrin (β-CD) and Nanosponges (NS) prepared with different cross-linking ratios and different drug loading ratios to enhance solubility and dissolution rate of Albendazole (ALB). **Materials and Methods:** Diphenyl Carbonate (DPC) was used as cross-linker for preparing NS with various β-CD and DPC ratios (1:2 and 1:4). Solvent evaporation was used to make binary complex. ALB and NS were dissolved in Dichloromethane (DCM) in 1:1 and 1:2 ratios and triturated until solvent evaporated. Phase solubility, saturation solubility and *in vitro* dissolution studies were performed. Solid state characterization as well as spectral and thermal analyses was done. **Results:** Stability constant for complexes ALB-β-CD, ALB-NS (1:2 ratios) and ALB-NS (1:4 ratios) were found to be $1715M^{-1}$±18.3, $1902M^{-1}$±29.5 and $1945M^{-1}$±30.1 respectively. Maximum solubility of all complexes was observed in fed state simulated intestinal fluid (FeSSIF). The increase was to the tune of 3-8 folds for all binary complexes at 1:1 and 1: 2 drug loading ratios. Dissolution rate increased by 47%-67% for drug loading ratio 1:1 and 55-71% for drug loading ratio 1:2 in FeSSIF in 150 min. **Conclusion:** β-CD based NS improved solubility of ALB. Presence of drug in molecular form in nanochannels and amorphization were responsible for increase in solubility. Nanosponges prepared in ratio 1:4 and drug loading in ratio 1:2 showed highest increase in solubility and dissolution rate.

Keywords: β-cyclodextrin, Binary complex, Nanosponges, Albendazole.

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INTRODUCTION

Albendazole (ALB) is **a** benzimidazole-derived anthelminthic drug effective against many helminthes. For more than two decades, it has been used to treat helminth parasites in humans and animals, such as nematodes, metacestodes and hydathodes.[1] ALB is teratogenic, embryotoxic and causes liver degeneration when taken in long-term therapy.[2] ALB is frequently the medicine of choice in ophthalmic, muscle or blood systemic circulation impairment cases. However, because of its low solubility, it is poorly absorbed through gastrointestinal tract and for systemic disorders the oral dose is high which produces gastrointestinal distress. Particle size reduction, molecular modification and solid dispersion have been investigated for solubility enhancement.[3] Increasing ALB solubility by forming complexes with CDs could improve drug bioavailability.[4] CDs are one of the most commonly used polymers to improve water solubility, bioavailability and dissolution rate of hydrophobic drugs.[3] CDs are cyclic oligosaccharides with 6-8 glucose units linked together by D-1,4 linkages. They are produced when starch reacts with the enzyme cyclodextrin glycosyl transferase enzyme (CGTase).[5] Externally CD molecules are highly hydrophilic, whereas inside their ring cavity, they are relatively hydrophobic. CDs have been reported to form inclusion complexes with number of drugs of appropriate size. They are highly suited for non-polar molecules in liquid or solid state which can get entrapped in the hydrophobic interiors of the CDs.[6] The stability constant of complexes plays a definitive role in the efficiency of inclusion complexation as moderate values enables the drugs to cross biological membranes easily.[7] Inclusion of poorly water-soluble drugs in α-CD, β-CD, and γ-CD has been widely reported.[8,9] β-CD is more popular because of its safety and low cost. Many pharmaceuticals have been complexed with β-CD to improve their solubility, bioavailability, safety and stability.[10] These include acetyl salicylic acid,[11] piroxicam,[12] ketoconazole,[13] ibuprofen,[14] ketoprofen,[15] tolbutamide,[16] ALB.[17,18]

Nanosponges (NS) are biocompatible and nanoporous carriers made from CD using crosslinkers such as DPC, Pyromellitic Dianhydride (PMDA), Carbonyl Diimidazole (CDI) and hexamethylene diisocynate.[19,20] These carriers have the ability to form inclusion complexes and non-inclusion complexes with both hydrophilic and lipophilic drugs.[21] Acute and repeat dose toxicity experiments by Shende *et al.* proved their toxicological safety.[22] *In vitro* cell line toxicity on various cell lines and hemolytic

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activity evaluations have further confirmed their safety.[23] The CD and crosslinker ratios can be changed to improve drug loading and provide a tailored release profile. NS can be made using melt extrusion or solvent evaporation method.[24,25] van der Waals forces and hydrogen bond interactions are causative factors in the complex formation.[26] For drugs such as telmisartan,[27,28] meloxicam,[29] curcumin,[30] efavirenz,[31] cefpodoxime proxetil,[32] acyclovir[33] and resveratrol,[34] NS have been used as carriers to improve solubility and stability. They have also been used to mask the taste of oseltamivir phosphate and gabapentin.[35] Antivirals, proteins, anti-inflammatory medicines and anticancer treatments such as camptothecin, tamoxifen, quercetin, temozolomide, doxorubicin and 5-fluorouracil have all been delivered using a controlled release nanoparticle system including NS.[23-36]

The present work involved comparison of solubility enhancement of ALB by complexation with β-CD and carbonyl NSs with different crosslinking ratios. The effect on solubility and dissolution of ALB at different drug-carrier ratios was also studied. UV spectroscopy, infrared absorbance spectra, XRD and SEM were used to characterize the complexes.

MATERIALS AND METHODS

Materials

ALB was obtained as a gift sample from Chempro Pharma Pvt. Ltd., Mumbai. DPC was purchased from Spectrochem Pvt. Ltd., Mumbai. β-CD was gifted from Analab Fine Chemicals, Mumbai (India). Other AR grade reagents and distilled water were used.

Synthesis of β-CD NS

NS with various molar ratios of β-CD and DPC (1:2 and 1:4) were synthesized. For 1:2 ratio (NS_2), 11.35 g of anhydrous β-CD and 4.28 g of DPC and for 1:4 ratio (NS_4), 11.35 g of anhydrous β-CD and 8.56 g of DPC were mixed thoroughly by trituration and gradually heated to 100°C with magnetic stirring for 5 hr in a thermostated vessel. Phenol crystals appeared as a byproduct of the reaction and were removed carefully. Unreacted β-CD and DPC were removed by washing NSs initially with Distilled Water (DW) and then with acetone.[37]

Evaluation of NS

The percentage practical yield was calculated for NS_2 and NS_4 ratio. Malvern Zetasizer (Model no: Nano ZS90) was used to determine the particle dimensions, zeta potential and polydispersity of the NSs. The measurements were done in distilled water.

Preliminary Evaluation of Complexes

Phase solubility studies

The phase solubility method of Higuchi and Connors was used to obtain the stability constants (Kc) and stoichiometric ratio of complexation. Excess of ALB was added to different millimolar (mM) ratios of β-CD, NS_2 and NS_4 and stirred for 24 hr at 37±0.5°C in an orbital shaker (Remi CIS-24BL). The dispersions were then filtered using Whatman filter paper 4 and drug concentration was measured using a UV Spectrophotometer (Make: Jasco V-730) at 295 nm. The stability constant was calculated from plot of the concentration of ALB (mM) versus the concentration of β-CD, $NS_2$and NS_4 (mM) respectively.[38]

Preparation of complexes

A previously reported solvent evaporation approach[39] was used to make binary complex (Table 1). In brief, ALB and NS were dissolved in DCM in 1:1 and 1:2 molar ratios, respectively and triturated until solvent evaporated. Gradual evaporation of the solvent is caused by frictional heat and turbulence generated during trituration. The wet complexes were dried in an oven overnight (at 50°C). The saturation solubility of DL_1-NS_2, DL_2-NS_2, DL_1-NS_4 and DL_2-NS_4 complexes was tested in various dissolution media with DL_1 indicating 1:1 drug: carrier complex and DL_2 indicating 1:2 loading.

Evaluation and Characterization of Complexes

Saturation Solubility Studies

Saturation solubility of ALB plain and in various complexes was determined in 20 mL of DW, 0.1 N HCl, phosphate buffer pH 6.8, fasting and fed state simulated intestinal fluid (FaSSIF and FeSSIF), and equilibrated in an orbital shaker (Remi CIS-24BL) at 37±0.5°C for 24 hr at 70 rpm.[40] After 24 hr the dispersions were filtered using a membrane filter (0.45 m) and ALB concentration was determined using UV Spectrophotometer (Make Model: Jasco V-730).[39] Statistical p-test was applied using the GraphPad InStat [DATASET1.ISD] software.

Fourier Transform Infrared Spectroscopy (FT-IR)

To analyze any interaction between ALB, β-CD, $NS_2$and NS_4 and to confirm formation of complexes, IR spectra of drug and binary complexes were recorded using Shimadzu FTIR (version 2.26) spectrophotometer. Spectra were scanned over a frequency range of 3600-650 cm^{-1}.

Field Emission Scanning Electron Microscopy (FESEM)

FESEM (Instrument name: FEI Nova Nano SEM 450) was used to determine the surface morphology of samples ALB, ALB-β-CD, DL_1-NS_2 and DL_1-NS_4 complexes. Magnification power of ALB-β-CD, DL_1-NS_2 and DL_1-NS_4 was 30,000x at pressure of 1.5-4 pa.

Differential Scanning Calorimeter (DSC)

Thermograms for ALB and binary complexes were obtained using DSC (Model: Mettler Toledo DSC 1). The heating rate was

10°C/min, with a temperature range of 30-300°C. Samples were analyzed in a nitrogen atmosphere at 40-60 mL/min.

Powder X-ray Diffraction (PXRD)

The PXRD spectra of ALB, ALB-β-CD, DL_1-NS_2 and DL_1-NS_4 complexes were recorded using powder X-ray diffractometer (Rigaku Analytical XRD, India) with K-beta filter. Scanning mode of 2θ/θ was used to obtain the diffractograms. The degree of crystallinity was calculated using the formula:

$$\text{Degree of crystallinity} = \frac{\Sigma C}{\Sigma C+Ea} \times 100 \quad \text{Eq.1.}$$

Where,

c= crystalline peak intensities.

a= amorphous peak intensities.

In vitro dissolution studies

USP type II dissolution apparatus (Lab India Dissolution Test Apparatus, DISSO 2000, and India) was used for dissolution studies in 900 mL of 0.1 N HCl, phosphate buffer pH 6.8 buffers, FaSSIF and FeSSIF at 37±0.5°C and 50 rpm paddle speed. At intervals of 30, 60, 90, 120 and 150 min, samples were analyzed by UV Spectrophotometer (Make Model: Jasco V-730) at 295 nm. The dissolution kinetics was studied using DDSolver: Add-In Program.[41]

Stability studies

In a stability chamber (CHM-65 REMI) set at 40°C and 70% RH, the drug-loaded NS were stored. The complexes underwent a 3-month evaluation of their physical characteristics, size and nature with a 1-month sampling frequency.

RESULTS AND DISCUSSION

Evaluation of NS

The percentage practical yield obtained for NS_2 and for ratio NS_4 was 68.71% w/w and 88.15% w/w respectively. In this work, NS were produced by crosslinking β-CD with DPC to create NS. The particle size of NS_2, NS_4, DL_1-NS_2 and DL_1-NS_4 was found to 656.1 nm, 844.6 nm, 1430 nm and 1.343e4 nm respectively. The polydispersity index of NS_2, NS_4, DL1-NS_2 and DL_1-$NS_4$was found to be 0.147, 0.253, 1.000 and 0.593 respectively. Zeta potentials for NS_2, NS_4, DL_1-NS_2 and DL_1-NS_4 found to be -4.13 mV, -0.0535 mV, -6.71 mV and -10.5 mV. The higher magnitude of repulsive forces suggested by the high zeta potential will lessen the probability for particle aggregation.[1]

Phase Solubility Studies

Phase solubility studies aid in determining the stoichiometry and potency of interaction between the drug and carriers. The phase solubility studies showed AL type curvilinear graphs of ALB with all complexing agents. This demonstrated the stoichiometric 1:1 formation of inclusion complex. Stability constant (Kc) was estimated as the slope of the linear part of the phase solubility curve. Good complexation capacity is indicated by Kc values above 150 M^{-1} (Table 2). All of the complexes showed a respectably strong level of complexation, with the ALB-NS_4 exhibiting the strongest level of ALB interaction.[1] Low values of stability constants indicate tendency for drug leakage from the complexes and very high values will restrict diffusion of drug from complexes.[23] ALB-NS_4 had a higher stability constant than plain NS_2 and β-CD. Higher stability constant in NSs can be attributed to more numbers of points of interaction between drug and NSs possibly due to inclusion complexation into β-CD and non-inclusion complexation into nanocavities created due to crosslinking.[33]

Evaluation and Characterization of Complexes

Saturation Solubility Studies of DL_1-NS_2 and DL_1-NS_4

Saturation solubility of plain ALB, ALB-β-CD, DL_1-NS_2 and DL_1-NS_4 in DW was found in the range of 9.371-32.24 µg/mL, respectively. In comparison to plain ALB in DW, the solubility of binary complexes with β-CD, NS_2 and NS_4 (p<0.001) was increased by 0.899, 2.277 and 3.440-fold respectively. In phosphate buffer pH 6.8, the solubility of binary complexes with β-CD, NS_2 and NS_4 (p<0.001) was enhanced by 2.101, 3.122 and 3.891-fold, respectively, when compared to plain ALB. In comparison to plain ALB in 0.1N HCl, the solubility of binary complexes with β-CD, NS_2 and NS_4 (p<0.001) was increased by 2.443, 3.388 and 5.808-fold respectively. When compared to plain ALB in FaSSIF, the solubility of binary complexes with β-CD, NS_2 and NS_4 (p<0.001) was enhanced by 2.382, 4.138 and 4.977-fold, respectively. When compared to plain ALB in FeSSIF, the solubility of binary complexes with β-CD, NS_2 and NS_4 (p<0.001) was enhanced by 2.946, 4.853 and 7.654-fold, respectively [Figure 1 (A)].

Saturation Solubility Studies of DL_2-NS_2 and DL_2-NS_4

Saturation solubility of plain ALB, ALB-β-CD, DL_2-NS_2 and DL_2-NS_4 in distilled water was found in the range of 6.966-34.556 µg/mL, respectively. In comparison to plain ALB in DW, the solubility of binary complexes with β-CD, NS_2 and NS_4 (p<0.001) was increased by 1.531, 3.206 and 4.960-fold respectively. In phosphate buffer pH 6.8, the solubility of binary complexes with β-CD, NS_2 and NS_4 (p<0.01) was enhanced by 1.279, 1.921 and 2.667-fold, respectively, when compared to plain ALB. In comparison to plain ALB in 0.1N HCl, the solubility of binary complexes with β-CD, NS_2 and NS_4 (p<0.001) was increased by 2.131, 4.020 and 6.723-fold respectively. When compared to plain ALB in FaSSIF, the solubility of binary complexes with β-CD, NS_2 and NS_4 (p<0.001) was enhanced by 1.238, 2.194 and 3.868-fold, respectively. When compared to plain ALB in FeSSIF, the solubility of binary complexes with β-CD, NS_2 and NS_4 (p<0.001)

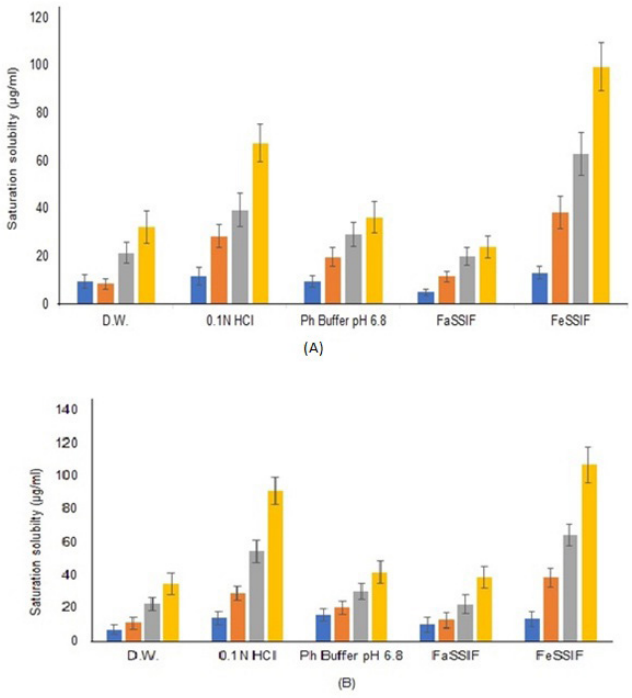

Figure 1: Saturation solubility studies for (A)DL_1 (B)DL_2.image1

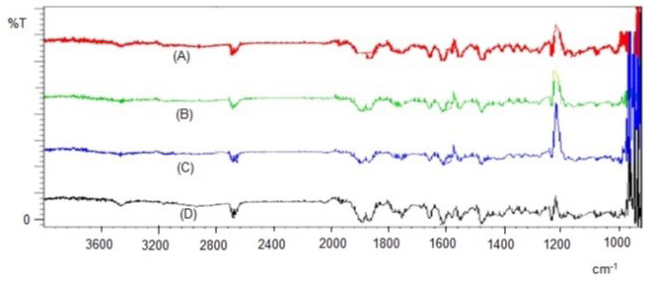

Figure 2: FTIR of (A)ALB (B)β-CD (C)NS_2 and (D)NS_4.

was enhanced by 2.904, 4.873 and 8.099-fold, respectively [Figure 1 (B)].

Fourier Transform Infrared Spectroscopy (FTIR)

To corroborate results, IR spectra of ALB and binary complexes were captured (Figure 2). The C-N stretch is visible in ALB's characteristic FTIR spectra at 2330.56 cm^{-1}. Carboxylic acid stretch is at 2652.0 cm^{-1} and alkanes stretch is at 1441.98 cm^{-1}. The Alkyl amine group's characteristic peak, at 1122.92 cm^{-1}, was visible in FTIR spectra of NS. FTIR studies supported complexation of ALB and NS. Distinctive peaks visible in the spectra of the plains NS and ALB were shifted, according to the IR spectra of the complex. FTIR spectra confirmed no interaction between NS and ALB.

Table 1: Abbreviations for complexes.

NS_2	Nanosponges (β-CD and DPC) in the ratio 1:2
NS_4	Nanosponges (β-CD and DPC) in the ratio 1:4
DL1-NS_2	ALB-NS2 complexes in the ratio 1:1
DL2-NS_2	ALB-NS2 complexes in the ratio 1:2
DL1-NS_4	ALB-NS4 complexes in the ratio 1:1
DL2-NS_4	ALB-NS4 complexes in the ratio 1:2

Table 2: Stability constants constants (Mean±SD, *n*=3)

Sr. no.	Complexing agent	Type of curve	Stability constants (Kc)
1	ALB-β-CD	AL	1715M^{-1} ± 18.3
2	ALB-NS (1:2)	AL	1902M^{-1} ± 29.5
3	ALB-NS (1:4)	AL	1945M^{-1} ± 30.1

Field Emission Scanning Electron Microscopy (FESEM)

SEMs of a few different formulations, including drug loaded ALB, β-CD, NS_2 and NS_4were taken. In Figure 3 the ALB's characteristic flat-shaped crystals may be seen. When a solid was dispersed with NS, the surface morphology significantly changed, showing that the drug had partially filled the NS's pores.

Differential Scanning Calorimetry (DSC)

The DSC spectra of ALB (Figure 4) exhibited a clear endotherm at 208°C, which corresponds to ALB melting point. The DSC thermogram of plain NS, ALB-β-CD, ALB-NS_2 and ALB-NS_4 all shows the significant difference. Inclusion complex of ALB with NS was indicated by the thermograms of binary complexes, which showed shallow and broadened peaks at about 208°C. This can be attributed to molecular dispersion of ALB in the NSs with lipophilic functional groups of drugs trapped inside the hydrophobic cavities.[1] The melting peak of the complex should become lesser when partial complexation takes place, indicating a drug-β-CD/NS interaction.

Powder X-ray Diffraction (PXRD)

Diffraction pattern of ALB reveals its crystalline nature, as seen by the distinctive peaks at diffraction angles at 7.297°, 17.857° and 25.879° (Figure 5). PXRD spectra were used to confirm the formation of NS. There was a noticeable reduction in the number and intensity of peaks in the diffractograms of complexes (Figure 5). The crystallinity of ALB in binary complexes was considerably less than plain ALB. The degree of crystallinity calculated by ratio of peak intensities of crystalline and amorphous forms revealed a significant decrease in crystallinity. It was found that the plain ALB, ALB-β-CD, ALB-NS_2 and ALB-NS_4 had degree of crystallinity of 59.53%, 50.31%, 40.81%, and 32.67% respectively. Beta-sitosterol inclusion complexes reportedly had

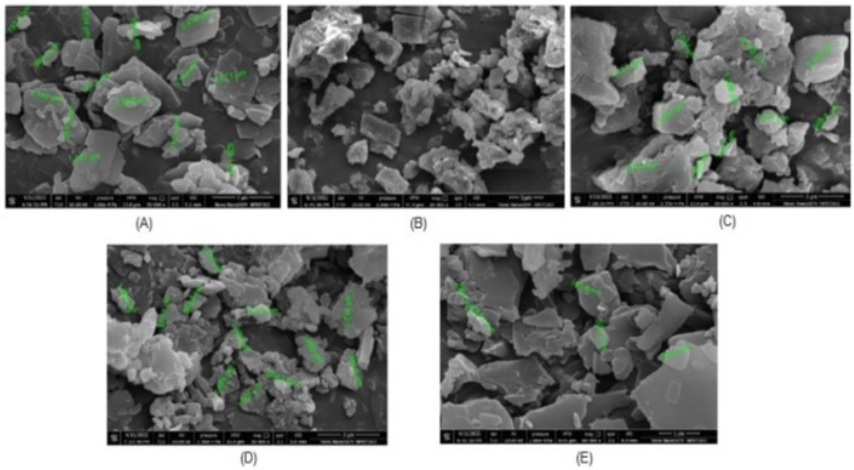

Figure 3: FESEM images of (A)DL_2-β-CD (B)NS_2 (C)DL_2-NS_2 (D)NS_4 (E)DL_2-NS_4.

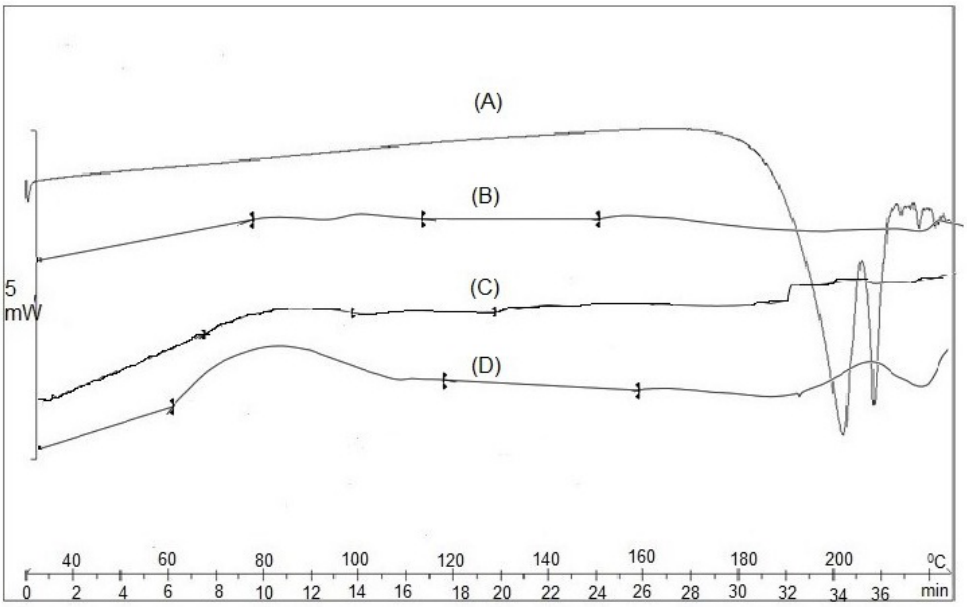

Figure 4: DSC analysis of (A)ALB (B)DL_2-β-CD (C)DL_2-NS_2 (D)DL_2-NS_4.

partial crystallinity.[1] They concluded that inclusion complexation may interfere with crystallization process leading to partial or complete amorphization. Amorphization can improve the solubility of drugs that are poorly soluble due to the lack of molecular orderliness in amorphous state.[41] However, due to their thermodynamic instability they need to be stabilized.[42] Thus, we may infer that NSs not only facilitate inclusion complexation of drug but also accord stability to amorphous ALB.

In vitro dissolution studies

In present studies all inclusion complexes showed faster release than plain ALB in various dissolution media (Figure 6). It was found that binary complexes with all NSs with different crosslinking ratios improved solubility and produced faster drug release. Release from NS_4 complexes was moderately higher than from NS_2 complexes. As crosslinking ratio increases drug entrapment is likely to be increased which can be the reason for increased dissolution rate. However the increase is moderate. Drug entrapment in inclusion complexation is dependent on molecular size and size of nanocavities.[43] The molar mass of ALB is 265.33 Daltons and we can presume that as crosslinking ratio increases the size of nanocavities decreases thereby affecting the entrapment of ALB.[44] It's also possible that some of the ALB does not undergo inclusion complexation and remains adhered to the surface of the NSs through hydrogen bonding with surface hydroxyl groups of CDs.[45] The physiological media affected drug release characteristics as well. In this instance, drug release was significantly slower in FaSSIF and faster in FeSSIF. This could be

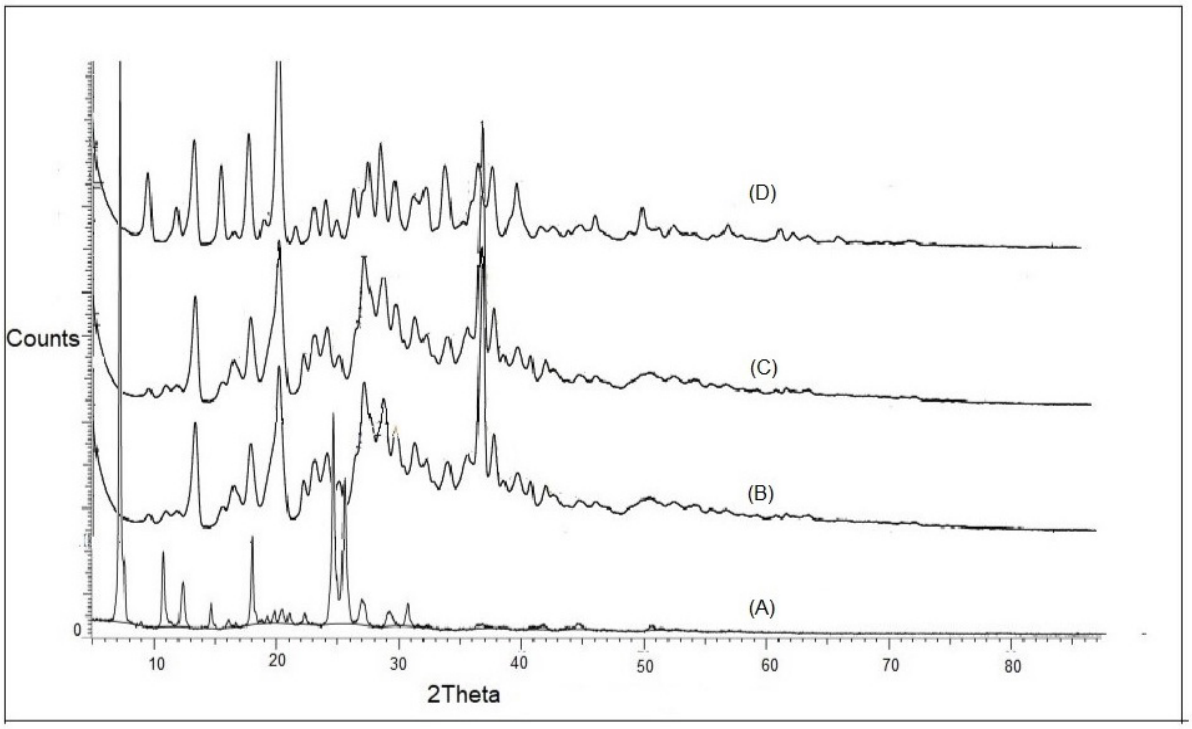

Figure 5: Powder XRD analysis of (A)ALB (B)DL_2-β-CD (C)DL_2-NS_2 (D) DL_2-NS_4.

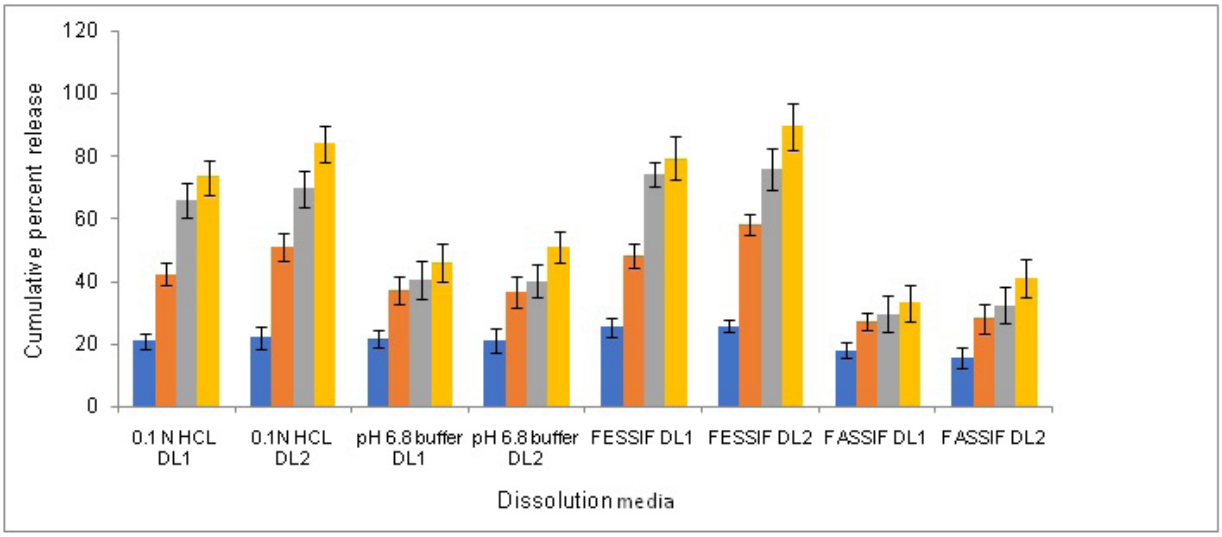

Figure 6: Release in various dissolution media at 150 min.

caused by pH-dependent solubility of ALB.[46] The percent drug release of plain ALB in all media was in the range of 15-25% in 150 min with least solubility in FaSSIF. The ALB-β-CD complexes displayed release in the range of 27-58%. The release of ALB in NS_1 and NS_2complexes was much higher than in β-CD in all media and for both drug loading ratios. Release in FeSSIF was found to be highest as compared to other media for all binary complexes. For binary complexes ALB-β-CD, DL_1-NS_2 and DL_1-NS_4, 48-79% of drug [Figure 7(A)], and for ALB-β-CD, DL_2-NS_2 and DL_2-NS_4, 58-89% of drug was released in FeSSIF over period of 150 min [Figure (B)].The release from ALB, ALB-β-CD, DL_1-NS_2 and DL2 was 18-33% [Figure (A)] and 15-41% from ALB-β-CD, DL_2-NS_2 and DL_2-NS_4 in FaSSIF [Figure (B)].21-73% of drug was released from ALB, ALB-β-CD, DL_1-NS_2 and DL_1-NS_4 [Figure 8(A)] and 22-84% from ALB-β-CD, DL_2-NS_2 and DL_2-NS_4 in 0.1 N HCl [Figure (B)]. For ALB, ALB-β-CD, DL_1-NS_2 and DL_1-NS_4, 21-46% of the drug was released [Figure (A)] and from ALB-β-CD, DL_2-NS_2 and DL_2-NS_4, 21-51% drug was released in

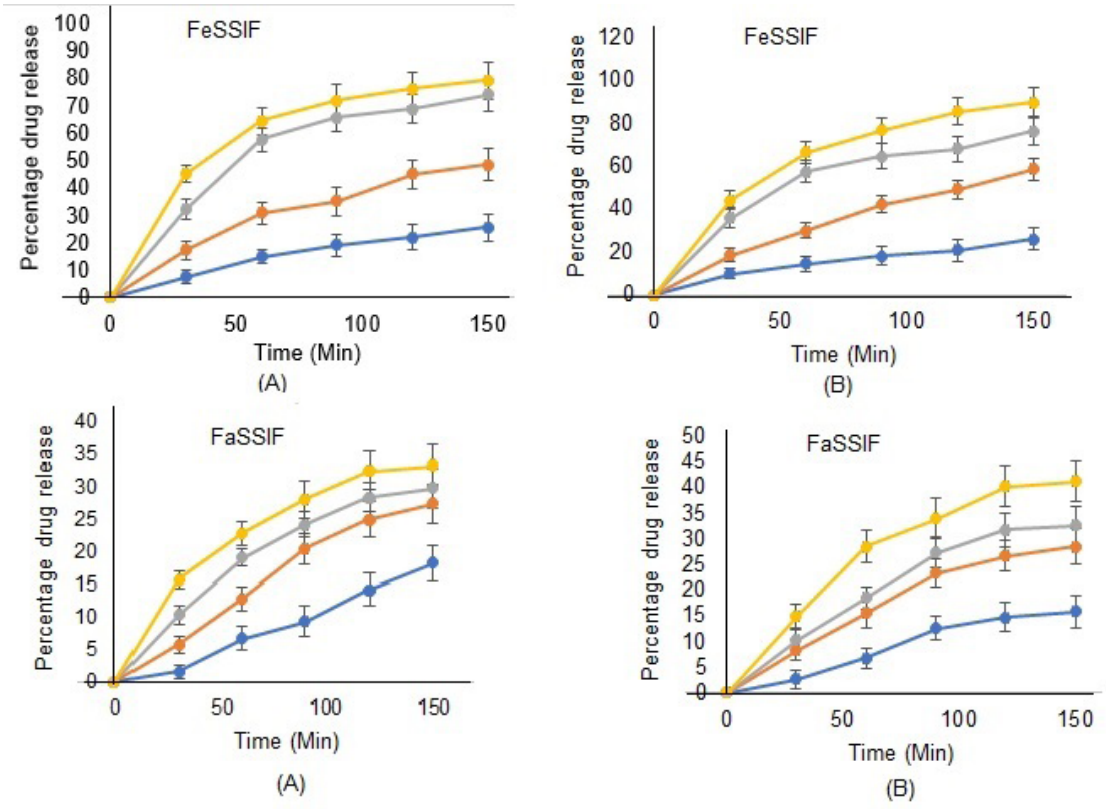

Figure 7: *In vitro* dissolution studies in FeSSIF and FaSSIF for (A)DL_1 (B)DL_2.image2

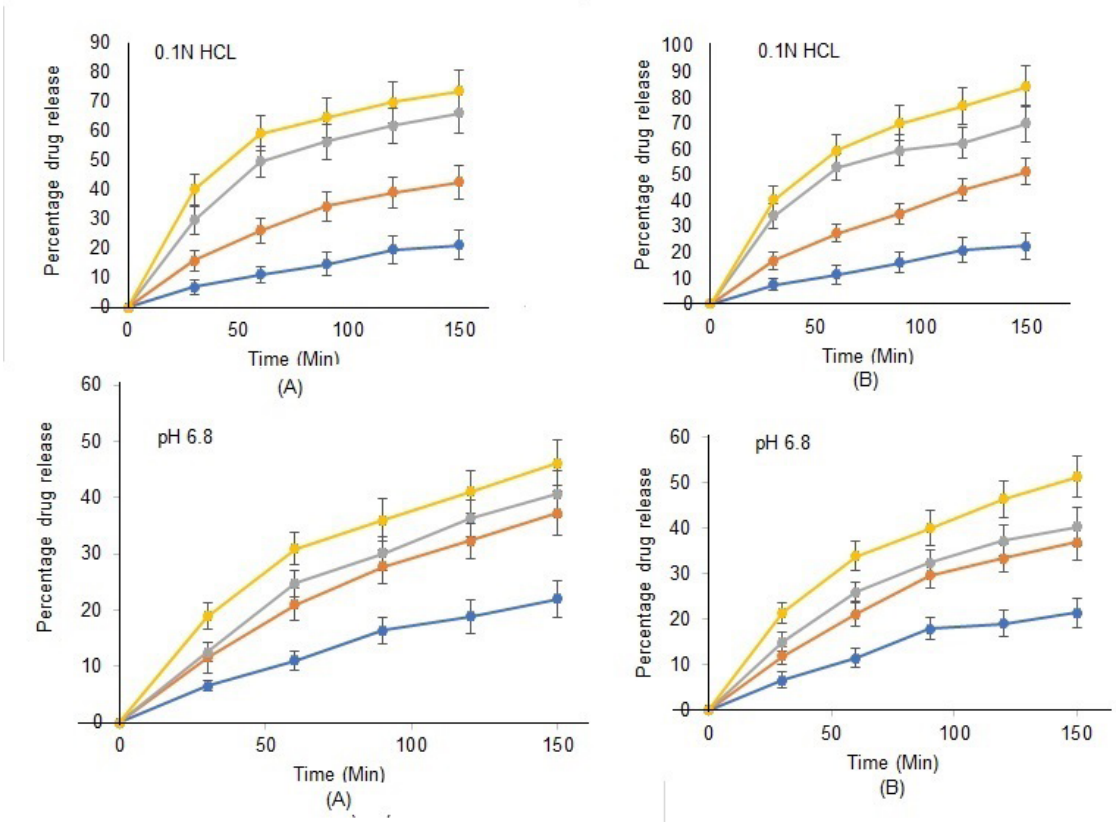

Figure 8: *In vitro* dissolution studies in 0.1N HCl and phosphate buffer pH 6.8 for (A)DL_1 (B)DL_2.image2

Table 3: Results obtained for various dissolution models

		0.1 N HCl	0.1 N HCl	Phosphate buffer pH 6.8	Phosphate buffer pH 6.8	FeSSIF		FaSSIF	
Model	Statistical parameter	NS_2	NS_4	NS_2	NS_4	NS_2	NS_4	NS_2	NS_4
Zero order	R^2 adj	0.703	0.759	0.8762	0.8425	0.979	0.979	0.919	0.856
	AIC	43.36	44.33	31.8195	35.8184	45.16	47.60	27.35	33.35
	MSC	0.169	0.091	0.9715	0.6446	3.248	3.207	1.544	0.839
1st Order	R^2 adj	0.926	0.983	0.9458	0.9432	0.072	0.123	0.959	0.935
	AIC	35.04	28.31	26.8616	29.6942	68.14	71.49	23.17	28.55
	MSC	1.217	2.760	1.7978	1.6653	0.582	0.773	2.240	1.639
Higuchi	R^2 adj	0.977	0.992	0.9901	0.9976	0.801	0.799	0.958	0.978
	AIC	27.88	23.63	16.6376	10.6805	44.89	41.14	23.43	21.86
	MSC	2.411	3.541	3.5018	4.8342	0.959	0.951	2.198	2.754
Hixson crowell	R^2 adj	0.875	0.949	0.9267	0.9171	0.852	0.827	0.948	0.914
	AIC	38.17	34.92	28.6752	31.9687	57.13	60.26	24.63	30.27
	MSC	0.696	1.659	1.4956	1.2862	1.253	1.098	1.997	1.352

phosphate buffer pH 6.8 [Figure (B)]. Higher solubility in FeSSIF can be attributed to presence of surface-active agents and its pH of 5.[47] Since ALB is observed to show pH dependent solubility both factors appear to contribute to faster and higher dissolution in FeSSIF than FaSSIF. The adjusted coefficient of determination (R^2adj), the Akaike Information Criterion (AIC) and the Model Selection Criterion (MSC) were computed by DDSolver for assessing the goodness of fit of a model. Based on the AIC values Higuchi model was found to be the best fit model for release from the NSs. The Higuchi model describes drug release from planar matrix systems and porous systems.[48] Though designed to explain release kinetics from modified release dosage forms, the NSs with their tortuous nanochannels can be considered to mimic modified release dosage forms and through which the molecularly dispersed drugs diffuse out into the surroundings. (Table 3).

Stability studies

Under accelerated conditions for 3 months, size, shape, or composition of drug in complexes did not change significantly. An analysis of NS stability at 40°C in both acidic and basic conditions confirmed these results. The stability of NS was unaffected by basic environment, however after two hours limited release of CD units was produced by the acidic environment (0.1 N HCl).[11]

CONCLUSION

The present study reports the use of β-CD based NS to enhance the solubility of the ALB, which is poorly soluble drug. Preparation, evaluation and characterization of the NS's binary complexes with ALB were carried out. Studies on spectral characterization showed that stable inclusion complexes were formed. Phase solubility studies revealed a linear increase in ALB's aqueous solubility with increasing NS concentration. The maximum *in vitro* drug release and saturation solubility was shown by the complex DL_2NS_4 in FeSSIF. The presence of the drug in molecular form in the nanochannels can be attributed to the increase in solubility. NS with different crosslinking ratios can be used as carriers for various applications like solubility enhancement.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

β-CD: β-cyclodextrin; **NS:** Nanosponges; **ALB:** Albendazole; **DPC:** Diphenyl carbonate; **DCM:** Dichloromethane; **FeSSIF:** Fed state simulated intestinal fluid; **FaSSIF:** Fasting state simulated intestinal fluid; **FT-IR:** Fourier Transform Infrared Spectroscopy; **FESEM:** Field Emission Scanning Electron Microscopy; **DSC:** Differential scanning calorimeter; **PXRD:** Powder X-ray Diffraction.

SUMMARY

The objective of the present study was to prepare and evaluate nanosponges ratios to enhance solubility and dissolution rate of Albendazole (ALB). Solvent evaporation method was used to make binary complex. The nanosponges were evaluated by *in vitro* method. β-CD based NS improved solubility of ALB. Presence of drug in molecular form in nanochannels and amorphization were responsible for increase in solubility. Nanosponges prepared in ratio 1:4 and drug loading in ratio 1:2 showed highest increase in solubility and dissolution rate.

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