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Soy Protein Isolate Blended with Cloisite 30B for Controlled Release of Anticancer Drug Vincristine

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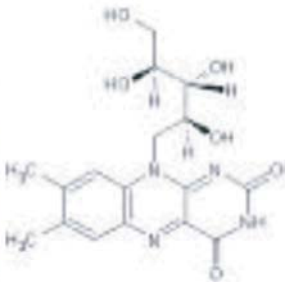
Abstract: In the present research program, soy protein isolate-sodium alginate hybrid composites were blended with cloisite 30B in aqueous solution. The TSP were characterized by various physicochemical techniques x-ray diffraction, Thormogravimetric analysis. From the X-ray diffraction we observed the amorophous nature of SPI. The results indicated that an intercalated or partially exfoliated nanocomposite could be achieved and the properties of the composite were significantly improved. The drug release kinetics were investigated using Vincrisine sulfate as the drug. The kinetics of the drug delivery system has been systematically studied. Drug release kinetics was analyzed by plotting the cumulative release data vs. time by fitting to an exponential equation which indicated the non-Fickian type of kinetics. The drug release was investigated at different pH medium and it was found that the drug release depends upon the pH medium as well as the nature of matrix.

Key words: SPI · Sodium alginate · Cloisite 30 B · Vincristine drug · Drug delivery Kinetics

INTRODUCTION

Soy Protein Isolate (SPI): Soy protein is a protein that is isolated from soybean. It is made from soybean meal that has been dehulled and defatted. Dehulled and defatted soybeans are processed into three kinds of high protein commercial products: soy flour, concentrates and isolates. Soy protein isolate has been used since 1959 in foods for its functional properties. Recently, soy protein popularity has increased due to its use in health food products and many countries allow health claims for foods rich in soy protein. It is generally regarded as being concentrated in protein bodies, which are estimated to contain at least 60–70% of the total soybean protein. Upon germination of the soybean, the protein will be digested and the released amino acids will be transported to locations of seedling growth. Soybeans contain a small but newly very significant 2S Albumin storage protein. Legume proteins, such as soy and pulses, belong to the globulin family of seed storage proteins called legumin and vicilins, or in the case of soybeans, glycinin and beta-conglycinin. It also contain biologically active metabolic proteins suchas enzymes, trypsin inhibitors, hemagglutinins and cysteine proteases very similar to papain. It is generally regarded as being concentrated in protein bodies, which are estimated to contain at least 60–70% of the total soybean protein The protein will be digested and the released amino acids will be transported to locations of seedling growth at the time of germination [1].

Structure of soybean



structure of soy protein isolate(SPI)

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Vincristine Sulfate Drug: Vincristine Sulfate Injection, USP (vincristine sulfate) is the salt of an alkaloid obtained from a common flowering herb, the periwinkle plant (*Vinca rosea*Linn). Originally known as leurocristine.. The molecular formula for Vincristine Sulfate, USP is $C_{46}H_{56}N_4O_{10}\bullet H_2SO_4$. It has a molecular weight of 923.04.0. Vincristine Sulfate, USP is a white to off-white powder. It is soluble in methanol, freely soluble in water, but only slightly soluble in 95% ethanol. In 98% ethanol, Vincristine Sulfate, USP has an ultraviolet spectrum with maxima at 221 nm (ε,+47,100). Vincristine Sulfate Injection, USP (vincristine sulfate) is a sterile, preservative-free, single use only solution available for intravenous use in 2 mL (1 mg and 2 mg) vials. Each mL contains 1 mg Vincristine Sulfate, USP, 100 mg mannitol and Water for Injection, USP q.s. Sulfuric acid or sodium hydroxide have been added for pH control. The pH of Vincristine Sulfate Injection, USP (vincristine sulfate) ranges from 4.0 to 5.0. At the time of manufacture, the air in the containers is replaced by nitrogen [2].

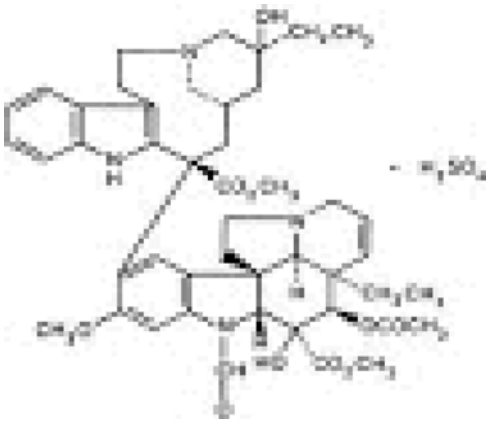

Fig 2: Structure of vincristine sulfate drug

MATERIAL AND METHODS

Experimental Studies: Soy protein isolate (Supro 760) with a protein content of 92.5% (dry basis) was obtained from Protein Technologies International (St. Louis, MO). Cloisite 30B were obtained from Southern Clay Products (Austin, TX). Vincristine sulfate drug was pursched from sigma Aldrich industries Ltd, india [3].

Preparation of Nanocomposite: One gram of soy protein isolate (SPI) was soaked in 50 ml deionized water and heated at 70°C to obtain a homogeneous solution. Nanoclay gram of soy protein was soaked in 50 ml deionized water and heated s% based on SPI) isolate are prepared by dispersing solutions with different clay compositions (1 wt %, 2wt% appropriate amounts of clays into 50 ml of soy protein isolate solution and vigorously stirring for 24 h. The mixtures were stirred continuously for 4 h and then cast onto level Teflon coated glass plates. After drying at room temperature for at least 72 h, the films were peeled from the plates [4].

Drug Loading: Vincristine sulfate drug of different loadings, i.e.1%, 2.5 wt %, 5 wt %, 7.5 wt % and 10 wt % were added to the SPI /Cloisite 30 B (1 wt %) clay solution and stirred for 1 h and then the polymer-drug conjugates were kept at room temperature for drying [5].

Haracterization:

X-Ray Diffraction (XRD): The d-spacing of Cloisite 30B corresponding to the diffraction peak at a 2θ angle of 5.0° was calculated to be 1.77 nm. There was no diffraction peak in the 2θ range of 2.5° to 10° for the

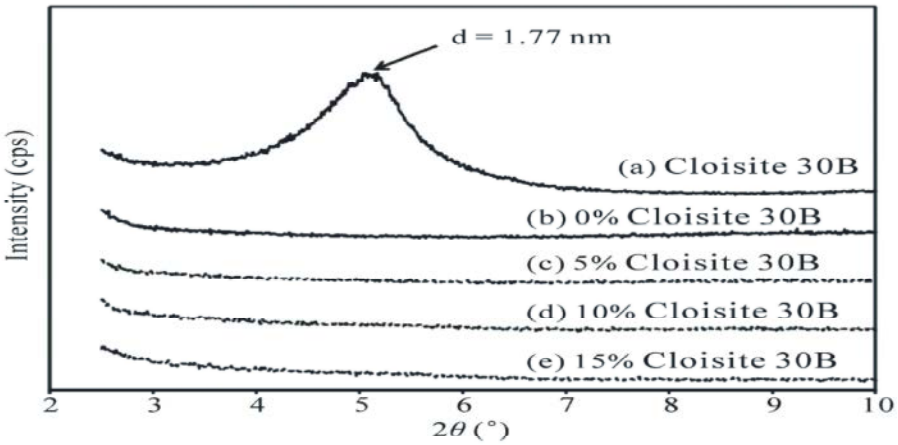

Fig: XRD patterns of Cloisite 30B bio-nanocomposites with different Cloisite 30Bcontents.

nanocomposites at all MMT contents of Cloisite 30B. There is no big peak in the X-ray diffraction studies. This proves that the smooth surface of soy protein isolate [6].

Scanning Electron Microscopy (SEM): The morphology of the fracture surface (cross-sectional surface) of the nanocomposite films were visualized using a field emission scanning electron microscope (JEOL 6400F, Japan Electron Optics Ltd., Tokyo, Japan) operating at 5 kV. Small pieces (0.5 × 0.5 cm) of bio-nanocomposite films were frozen in liquid nitrogen, cut using a sharp razor blade and mounted on specimen stubs with 2 sided carbon tape. The fracture surfaces of the films were sputter-coated with a thin layer (~8 - 10 nm) of gold-palladium (Au-Pd) using a sputter-coater (Hummer II, Anatech Ltd., Union City, CA). After coating, the samples were viewed under the scanning electron microscope [7].

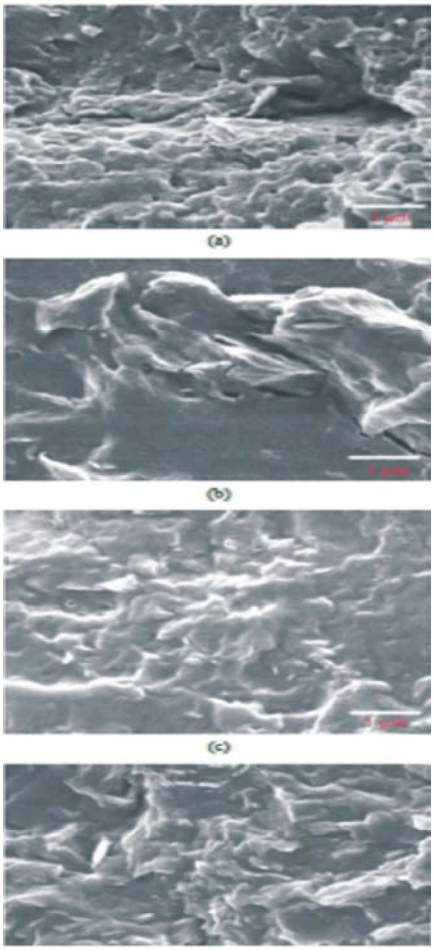

Fig: SEM of Cloisite30B bio-nanocomposites with different Cloisite 30Bcontents((a) 0%,(b) 5%, (c)10%, (d)15%).

Thermal Stability: The thermal stability of nanocomposite films were investigated using a thermogravimetric analyzer (Pyris 1 TGA, Perkin Elmer, Shelton, CT). The temperature of the sample was increased from room temperature to 900°C at a heating rate of 20°C/min. Weight loss of the sample was measured as a function of temperature. Three parameters were determined from the TGA data: the temperature at 10% weight loss, the temperature at 50% weight loss and the yield of charred residue at 850°C [8].

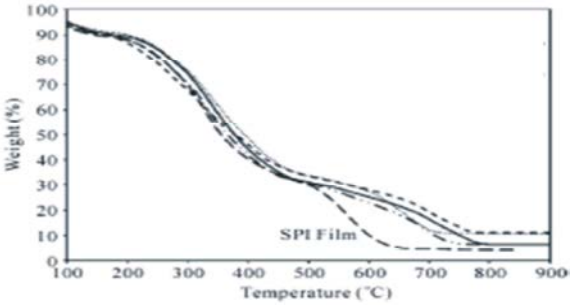

Fig: TGA curves of SPI/cloisite 30B.

RESULTS AND DISCUSSION

Dissolution Experiments: DissolutionLab India, Mumbai, India) equipped with six paddles at a experiments were performed at 37°C using the dissolution tester (Disso test, paddle speed of 100 rpm. About 900 mL of phosphatebuffer solution (pH 3.4 and 7.4) was used as the dissolution media to stimulate gastrointestinal tract (GITconditions. A 5 mL aliquot (polymer–drug conjugate) was used each time for analyzing the curcumin content at a fixed time interval. The dissolution media was replenished with a fresh stock solution[9]. The amount of curcumin released was analyzed using a UV spectrophotometer (Systronics, India) at the *k* max value of 420 nm. Drug release mechanism from matrices From time to time, various authors have proposed several types of drug release mechanisms from matrices. various authors have proposed several types of drug release mechanisms from matrices. It has been proposed that drug release from matrices usually implies water penetration in the matrix, hydration, swelling, diffusion of the dissolved drug (polymer hydrofusion) and /or the erosion of the gelatinous layer. Several kinetic models relating to the drug release from matrices, selected from the most important mathematical models, are described over here. However, it is worth mentioning that the release mechanism of a drug would depend on the dosage from used [10].

Zero-Order Kinetics:

$W = k1\ t$

First-Order Kinetics:

$\ln (100- W) = \ln 100 - k2\ t$

Hixon-Crowel's Cube- Root Equation (Erosin Model):

$(100- W)\ 1/3 = 100\ 1/3 – k3\ t$

Higuchi's Square Root of Time Equation (Diffusion Model):

$W = k4\ t$

Power Law Equation (Diffusion/ Relaxation Model):

$Mt / M8 = K^5 t_n$

Mt/M8 is the fractional drug release into dissolution medium and k5 is a constant incorporating the structural. and geometric characteristics of the tablet. The term 'n' is the diffusional constant that characterizes the drug release transport mechanism. When 0.5, the drug diffused and released from the polymeric matrix with a quasi-Fickian diffusion mechanism. For n > 0.5, an anomalous, non-Fickian drug diffusion occurs. When n = 1, a non-Fickian, case II or Zero-order release kinetics could be observed [11].

In vitro Drug Release

Effect of pH, Time and Drug Loading: To investigate the effect of pH on the swelling of soy protein/C 30B composite (2.5%), we have measured the % cumulative release in both pH 1.2 and 7.4 media. Cumulative release data presented in Figure 8, 9 indicate that by increasing the pH from 1.2 to 7.4, a considerable increase in the cumulative release is observed for all composites. From it is seen that the 50 % drug-polymer composites have shown longer drug release rates than the other composite. Release data showed that formulations containing highest amount of drug displayed fast and higher release rates than those formulations containing

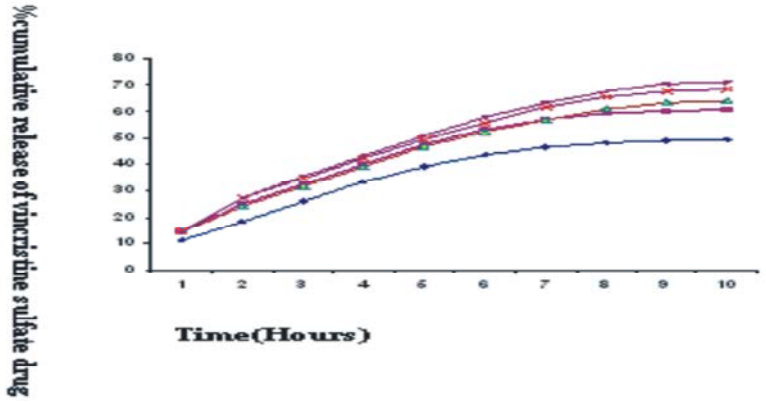

Fig 7: % cumulative release of vincristine sulfate drug vs time with different drug loadings of SPI at PH 1.2

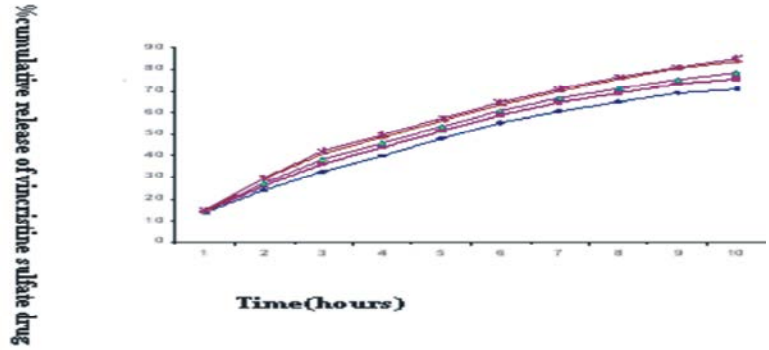

Fig 8: % cumulative release of vincristine sulfate drug vs time with different drug loadings of SPI at PH 7.4

Values of "k"			Values of "n"		Coordination Coefficient, R^2	
Sample code	pH 7.4	pH1.2	pH7.4	pH 1.2	pH7.4	pH1.2
1%wt	0.43	0.01	0.53	0.67	0.9321	0.9765
2.5wt%	0.54	0.04	0.63	0.65	0.974	0.976
5wt%	0.48	0.06	0.67	0.68	0.954	0.966
7.5wt%	0.58	0.11	0.71	0.87	0.907	0.955
10 wt%	0.60	0.16	0.88	0.96	o.911	0.957

a small amount of drug loading. The release rate becomes quite slower at the lower amount of drug in the matrix, due to the availability of more free void spaces through which a lesser number of drug molecules could transport [12].

Drug Release Kinetics: Drug release kinetics was analyzed by plotting the cumulative release data vs. timeby fitting to an exponential equation of the type as represented below [14]. M / M = kt removal of the device. Further, if the polymer degrades Here, M / M represents the fractional drug releasen at time t, k is a constant characteristic of the drug-polymer system and n is an empirical parameter character the release mechanism [13]. Using the least square sizing procedure, we have estimated the values of n and k for all the five formulations and these data are given in Table 1. [14] The values of k and n have shown a depends on the, % drug loading and polymer content of the matrix.once Values of 'k' for composites prepared by varying the amounts of drug containing and keeping/C 30B (2.5 wt %) constant, ranged from 0.43 to 0.60 in pH 7.4 and 0.01 to 0.16 in pH 1.2 respectively[14]. However, the drug-loaded composites exhibited 'n' values ran from 0.53 to 0.88 in pH 7.4 and 0.67 to 0.96 in pH 1.2 The value of less than 1 has also been recently aging, indicating a shift from erosion type release to a swelling controlled, non-flow micro viscosity inside the matrix and closure of non- fickian type mechanism was reported. This may be due to a reduction in the regions of cavities during the swollen state of the polymer. Similar findings have been found elsewhere, where in the effect of different polymer ratios on dissolution kinetics was investigated [15].

CONCLUSION

Novel composites of Soy protein isolate (SPI), cloisite 30B and Vincristine sulfate Drug were characterized by X-ray Diffraction and thermo gravimetric analysis. The drug release was monitored by changing time, % drug loading and pH of the medium. Here, We observed the non-Fickian type of Drug release.

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