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Research Article

Tamarind Seed Polysaccharides Blended with Cloisite 30B for the Controlled Release of Anticancer Drug Vincristine

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Abstract

In the present research program, tamarind seed polysaccharides (TSP) was blended with Cloisite 30B in aqueous solution. The TSP was characterized by various physicochemical techniques such as FTIR, X-ray diffraction, thermogravimetric analysis and SEM studies. From the X-ray diffraction it was observed the amorphous nature of TSP and from FTIR also observed different groups presnt in TSP. 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 anticancer drug vincristine sulfate . The kinetics of the drug delivery system was 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.

Keywords: TSP, Nano Composite, Cloisite30B, Vincristine , Drug delivery, Kinetics

Introduction

Tamarind seed polysachharide (TSP), derived from the seeds of *Tamarindus indica linn*., a common and most important tree of India and Southeast Asia, is composed of (1-4)-b-D-glucan backbone substituted with side chains of a-D-xylopyranose and b-D-galactopyranosyl (1→2)-a-D-xylopyranose linked (1→6) to glucose residues. The glucose, xylose, and galactose units are present in the ratio of 2.8/2.25/1.0. The molecular weight of tamarind seed polysaccharide (TSP) is within the range of 2.5×10^5 to 6.5×10^5 It can spread in water easily and change to mucilaginous liquid when heated up, as an acid and thermal resistant solution. Tamarind seed polysaccharide can change into gel in neutral and acidic pH. The gel can be used as a thickening and stabilizing agent in food industry [1].

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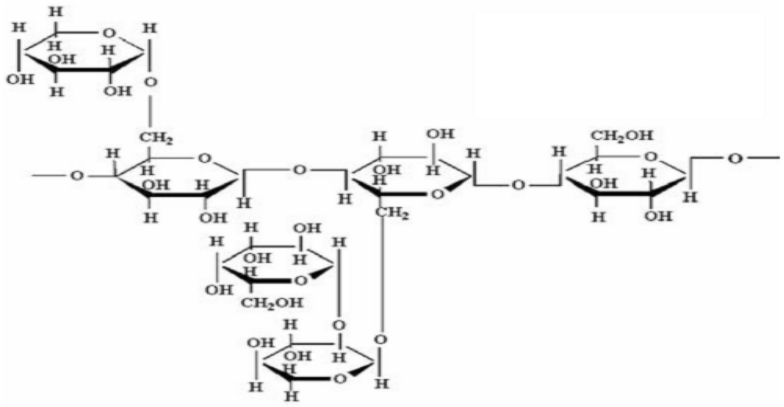

Figure 1.Structure of tamarind seed polysaccharides

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 KLeurocristine. The molecular formula for Vincristine Sulfate, USP is $C_{46}H_{56}N_4O_{10}•H_2SO_4$. 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].

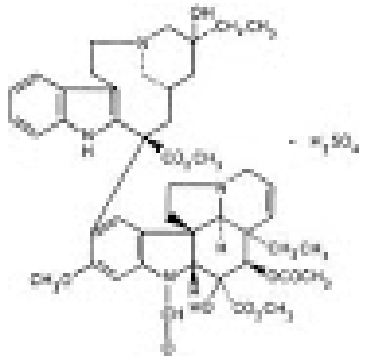

Figure 2.structure of vincristine sulfate drug

Materials and Methods

Experimental Studies: Tamarind kernel powder was obtained as gift sample from Sri Balaji Industries; Bangalore. Cloisite 30B was procured from Southern Clay Products, USA. Vincristine sulfate drug was purchased from Sigma Aldrich Industries Ltd,India [3].

Preparation of Nanocomposite: One gram of tamarind seed polysaccharide powder was soaked in 50 ml deionized water and heated at 70°C to obtain a homogeneous solution. Nanoclay and tamarind seed polysaccharides with with different clay compositions (1 wt %, 2wt%) appropriate amounts of clays into 50 ml of Tamarind seed polysaccharides solution and vigorously stirring for 24 h and cast into teflon coated plate . 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 TSP -Cloisite 30 B clay solution and stirred for 1 h and then the polymer-drug conjugates were kept at room temperature for drying [5].

Characterization

Fourier Transmission Infra Red Spectroscopy (FTIR)

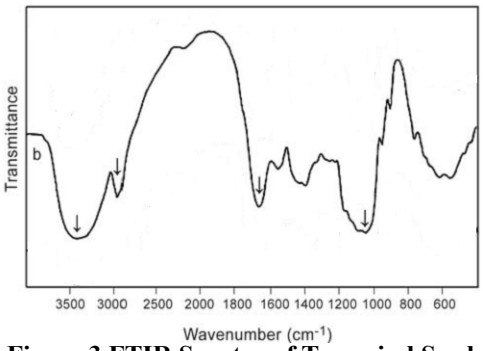

Figure 3.FTIR Spectra of Tamarind Seed Polysaccharide (TSP)

Figure-3 shows the FTIR spectrum of tamarind seed polysaccharide (TSP) that a band at 1648 cm^{-1} is attributed to the absorption band of the carbonyl (-C=O) stretching [8]. From the figure we revealed that each monosaccharide of tamarind gum has two isomers, comprising of a ring system and a chain system, which results in the appearance of the carbonyl absorption band. The other band at 1041 cm^{-1} that was assigned to the stretching vibration of (CH-OH) and other peaks that is -OH group present at 3400 cm^{-1} and peak attributed to the $–CH_2$ group present 2926 cm^{-1} [6].

Thermogravimetric Analysis

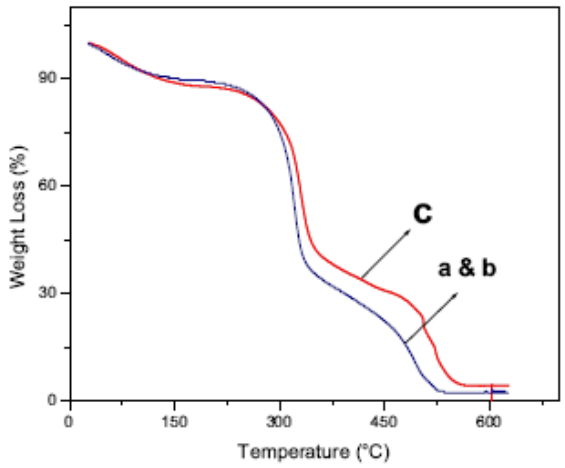

Figure 4.ThermogravimetricAnalysis of Tamarind seed polysaccharides

This figure-4 shows that the thermogravimetric analysis of tamarind seed polysaccharides at a temperature ranging from 30 °C to 500 °C in nitrogen atmosphere at the rate of 10 °C/min was performed to examine the thermal stability of different types of films and their TGA curves. From the thermogram of TSP it is observed that the thermogram breaks at three stages. The first break around 150°C is due to the absorbed water molecules in the sample. The second break around is due to the breakage of the weak bond between the a-D-xylopyranose molecules. The third break may be due to the internal cleavage of the D-xylopyranose molecules forming water and carbon dioxide gases[7].

Morphology

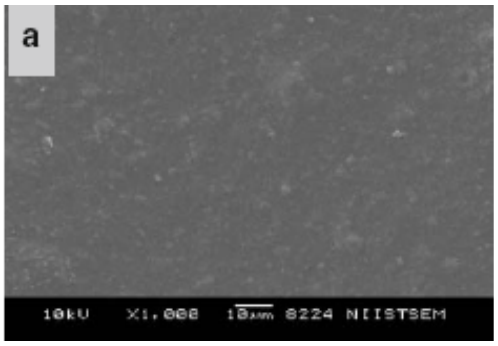

Figure 5.SEM of Tamarind seed polysaccharides (TSP)

The fig-5 shows that the SEM of TSP , It indicates the smooth and homogeneous surface of neat TSP [8].

X-Ray Diffraction (XRD)

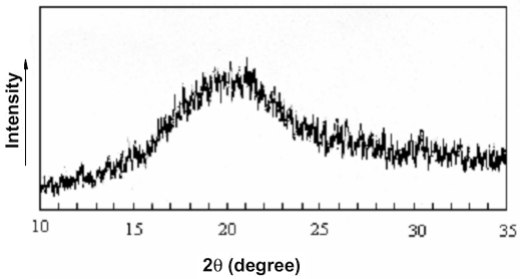

Figure 6.X-ray diffraction pattern of tamarind seed polysaccharide

Figure -6 shows the X-ray diffraction analysis of TSP . it It does not show any characteristic peak, which indicates that the structure is completely amorphous. . The results show that the isolated polysaccharide has similar behavior with that reported by others. [9]

Results and Discussion

Dissolution Experiments: Dissolution Lab 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 phosphate buffer 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. The amount of drg released was analyzed using a UV spectrophotometer (Systronics, India) at the *lamda* max value of 420 nm.

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 hydro fusion) 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 (1)

$W = k_1 t$

First - Order Kinetics (2)

$\ln(100- W) = \ln 100 - k_2 t$

Hixon-Crowel's Cube- Root Equation (Erosin Model) (3)

$(100- W)\ 1/3 = 100\ 1/3 – k_3 t$

Higuchi's Square Root of Time Equation (Diffusion Model) (4)

$W = k_4 t$

Power Law Equation (Diffusion/ Relaxation model) (5)

$Mt / M8=k5t\ n$

Mt/M*8* is the fractional drug release into dissolution medium and k_5 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 n is 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 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 tamarind seed polysaccharides/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 Figures 7, and 8 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 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].

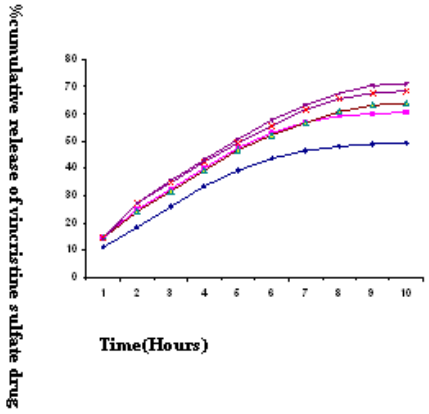

Figure 7.% cumulative release of vincristine sulfate drug vs. time with different drug loadings of TSP at PH 1.2

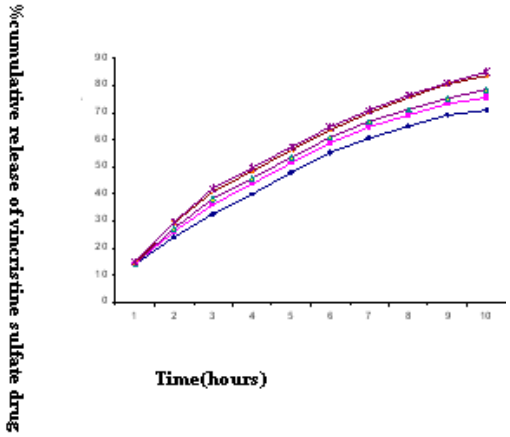

Figure 8.% cumulative release of vincristine sulfate drug vs. time with different drug loadings of TSP at PH 7.4[13]

Values of "k"			Values of "n"		Coordination Coefficient, R^2	
Sample code	pH 7.4	pH 1.2	pH 7.4	pH 1.2	pH 7.4	pH 1.2
1%wt	0.08	0.25	0.50	0.48	0.9800	0.9802
2.5wt%	0.04	0.07	0.54	0.55	0.9760	0.9853
5wt%	0.07	0.20	0.66	0.56	0.9820	0.9702
7.5wt%	0.25	0.34	0.67	0.67	0.9750	0.9872
10 wt%	0.29	0.40	0.74	0.89	0.9680	0.9882

Drug Release Kinetics: Drug release kinetics was analyzed by plotting the cumulative release data vs. time by fitting to an exponential equation of the type as represented below [14].

$M / M = k_t n$ Here, M / M represents the fractional drug release n 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 0.08 to 0.29 in pH 7.4 and 0.25 to 0.40 in pH 1.2 respectively[14] . However, the drug-loaded composites exhibited 'n' values ran from 4.2 to pH 7.4 and 0.48 to 0.89 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, wherein the effect of different polymer ratios on dissolution kinetics was investigated [15] .

Conclusion

TSP-vincristine sulfate drug was v produced by a casting/ solvent evaporation method wiith Vincristine sulfate Drug , an anticancer drug as a model drug. The chemical and morphological characterizations showed that there is a good compatibility between the matrix film and the drug used due to both kinds of strong interactions namely hydrogen bonds and ionic. The FTIR, X-ray diffraction,thermogravimetric studies and SEM of TSP was studied. Here we also observed non-fickian release of vincristine sulfate drug from the matrix

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