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FABRICATION AND IN-VITRO EVALUATION OF SPI-FURFURAL-MMT NANOCOMPOSITE DRUG DELIVERY SYSTEMS

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ABSTRACT

Biodegradable nanocomposites for regulated drug administration utilizing soy protein isolate (SPI) cross-linked with furfural and reinforced with montmorillonite (MMT) clay are the subject of this work. The structural and surface qualities of five different formulations were studied, each with a different amount of clay. According to the findings, the nanocomposites' stability and homogeneity were enhanced as the clay percentage increased. The nanocomposites were designed to mimic the environment of the gastrointestinal tract, therefore researchers included the antibacterial medication cefadroxil and performed in-vitro release trials under various pH settings. Researchers discovered that the amount of clay, pH, and polymer matrix all have a role in the release of drugs, with alkaline circumstances resulting in greater release rates. Drug release data analysis revealed a hybrid process including polymer relaxation and diffusion.

I. INTRODUCTION

The development of more effective drug delivery methods has spurred a dramatic shift in the pharmaceutical and therapeutic industries, highlighting the critical need of regulated, precise, and time-efficient distribution of bioactive compounds. Poor bioavailability, fast drug breakdown in physiological settings, systemic adverse effects, and non-specific targeting are some of the disadvantages of traditional drug delivery techniques, such as oral or parenteral routes. Because of these difficulties, scientists are always looking for new carrier systems that will improve the medications' stability, solubility, and therapeutic effectiveness while reducing their side effects. Because of its adaptability, biodegradability, and biocompatibility, biopolymer-based nanocomposite systems have stood out as an encouraging category of materials among the several approaches investigated. The natural origin, availability, and superior film-forming capabilities of soy protein isolate (SPI) have made them a particularly attractive candidate for use as drug delivery matrices in nanocomposites.

Highly functional proteins like glycinin and β-conglycinin make up soy protein isolate. These proteins may create three-dimensional networks through electrostatic forces, hydrophobic interactions, and hydrogen bonding. For its inherent qualities, SPI is a great material to work with for creating stable hydrogels and nanocomposite films for use in medicine. Furthermore, SPI offers a flexible framework for regulated release of drugs due to its reactive amino acid residues, which permit chemical changes, cross-linking, and the insertion of bioactive compounds. Achieving prolonged drug release, preserving sensitive molecules from degradation, and improving drug solubility are all crucial for current therapeutic interventions, and SPI-based nanocomposites have demonstrated promising results in these areas.

The high aspect ratio, huge surface area, and good intercalation capabilities of MMT, a naturally occurring multilayer silicate, allow it to interact strongly with polymer matrices. Encapsulated medicines can have their release kinetics modulated and their structural integrity provided by MMT when disseminated inside SPI networks. Intercalation of bioactive compounds into MMT's layered structure improves drug loading efficiency and prevents drugs from diffusing too quickly. The formation of convoluted routes by MMT nanoclay can impart controlled release behavior, which is especially useful for attaining

prolonged therapeutic benefits over extended durations, by slowing down drug migration.

A novel method for cross-linking and functionalizing protein-based matrices is offered by including furfural, a naturally produced aldehyde from agricultural leftovers, alongside SPI and MMT. Nanocomposites made from furfural have improved thermal stability and structural stiffness thanks to Schiff base connections formed when furfural's aldehyde groups react with amino groups in proteins. Crucial aspects for drug release applications, including as swelling behavior, porosity, and degradation profile, are modulated by this chemical cross-linking, which also reinforces the SPI matrix. Additionally, furfural-based cross-linking is seen as eco-friendly, which fits nicely with the growing focus on sustainable materials and green chemistry in pharmaceutical research. Researchers can build a synergistic nanocomposite system with improved mechanical characteristics, controlled release profiles, and drug encapsulation efficiency by mixing SPI, MMT, and furfural.

In line with the present trend of developing smart, responsive, and multifunctional carriers for targeted therapies, SPI-furfural-MMT nanocomposite drug delivery systems have been developed. By modifying these systems in response to changes in pH, temperature, or enzyme activity, it is possible to minimize systemic toxicity while achieving site-specific drug release. For example, in some enzymatic settings or the acidic stomach environment, the protein matrix might undergo conformational changes that release the drug from its capsule at the target location. Treatment of chronic illnesses, cancer, and infections relies on cellular uptake, bioavailability, and penetration into target tissues, all of which are improved by the nanoscale size of these composites.

II. REVIEW OF LITERATURE

Kamala Kumari, Paravastuet al., (2019) The study of nanocomposites has recently emerged as an exciting new field of study. Polymer nanocomposites and clay nanocomposites are the two main categories of nanocomposites. Polymer nanocomposites that enhance mechanical qualities are now a hotspot for research and development in the vast subject of nanotechnology. In the field of polymer research, clay nanocomposites have emerged as front-runners due to their ability to enhance additional capabilities. On the other hand, a great deal of other important sectors are attracting attention at the moment or are about to. Because of their surface and rheological characteristics, nanocomposites have the potential to be

utilized as drug carriers. Among the many significant topics covered in this study are the technological aspects of claypolymer based nanocomposites, which have a wide range of potential uses in fields as diverse as biomedicine, electrical and electronic engineering, fuel cells, and flammability resistance.

Elsayed, nadiaet al., (2018) The Montmorillonite/Montmorillonite (MMT) clay was modified using an ammonium chloride modifier to produce a polypropylene nanocomposite, which was then mixed with hydrogenated clay and tallow. The thermal gravimetric analysis (TGA), scanning electron microscopy (SEM), and Fourier-transform infrared (FTIR) were used to analyze the produced nanocomposite. Mechanical characteristics, water absorption, and scanning electron microscopy (SEM) were used to describe the fibers that were created using the melt spinning process. The fibers were either pure polypropylene (PP) or a polypropylene/montmorillonite clay nanocomposite (PP/MMT). The results demonstrate that the nanocomposite fibers outperform pure polypropylene fibers in regards to thermal stability, mechanical characteristics, and water absorption. What's more, the nanocomposite exhibits a high degree of homogeneity between the polypropylene and MMT clay components. The solvent immersion approach was used to successfully load ibuprofen (IBU) into nanocomposite fibers made of polypropylene and polypropylene/montmorillonite clay. The drug fiber ratio was varied, and a glyoxal cross linker was also present. within 120 minutes of monitoring the drug release profile, it was found that within an hour of initiating the release, the fiber had released around 33% of the initial loaded medication.

Nayak, Preetishreeet al., (2011) The melt extrusion process was used to combine soy protein isolate with varying percentages of MMT in order to create nanocomposites. The nanocomposites were examined utilizing techniques such as XRD, TEM, SEM, and TGA. Research using XRD showed that the bio-nanocomposites did not have any diffraction peaks. A higher MMT concentration was associated with a more severe exfoliation, according to the TEM studies. Through scanning electron microscopy (SEM), the morphology of the nanocomposites was determined. The TG analysis was used to assess the nano-composites' deterioration pattern. In order to study the nanocomposites' drug delivery mechanism, researchers mixed them with ofloxacin in various pH environments. We theorized the drug delivery mechanism based on the kinetic data and analyzed the various kinetic parameters.

Sasmal, Abhisek et al., (2009) A mixture of organoclay Cloisite 30B and furfural, a bio-based

aldehyde, has been used to cross-link soy protein isolate. The FTIR data has been used to determine the cross-linking process. The X-ray diffraction analysis revealed the structure and apparent interlayer spacing of the SPI/ MMT nanocomposites that were created using solution intercalation. The TGA technique has been used to track the cross-link product's deterioration trend. The kinetic parameters have been evaluated using a computerized LOTUS package approach. The kinetic data has been used to discuss the degradation process of the nanocomposites. The nanocomposites have also been shown to be biodegradable.

III. MATERIALS AND METHODS

Materials

A well-respected Indian business supplied the food-grade soy protein isolate (SPI), which has a protein content of about 90%. The analytical reagent (AR) grade furfural and propionic acid were bought from Merck India and used without additional purification. Closite 30B, a sodium-based montmorillonite (MMT) clay, was purchased from the authorized distributor in India of Southern Clay Products. Ranbaxy Laboratories Ltd. (India) supplied the model medicine cefadroxil, and it was used exactly as received.

Preparation of cross-linked SPI

About 50 gm of soy protein isolate (SPI) was in 500 ml of deionized water. Furfural (5% (w/w) dry base of SPI) was added drop by drop to the slurry while a mechanical stirrer agitated it. Calculated MMT (C30B) was added to this slurry (1.25%, 2.5%, 5%, 7.5%). The mixture was mixed for 10 hours at room temperature and left for 18–24 hours.

The slurry was centrifuged (Sorvall Superspeed RC2-B; 4541g, 10min) to remove excess water, and the residue was dried at <50°C in a convection oven. Milled dried modified SPI passed through a 35-mesh sieve. The material's moisture was measured withSartorious Moisture Analyzer. For this investigation, montmorillonite (MMT) clay was varied while soy protein isolate (SPI) and furfural were kept constant to create five formulations. AS-01, the original formulation, included SPI and 10% furfural without clay. AS-02 and AS-03 have 1.25% and 2.5% clay, respectively. AS-04 has 5% clay and AS-05 7.5%: the most. The nanocomposites' characteristics were studied by increasing clay content, since all formulations included 10% furfural and the rest SPI.

Preparation of cefadroxil-loaded cross-linked product

The required amount of SPI-furfural nanocomposite (AS-04) was in 5 ml deionized water. A mechanical stirrer continually churned the paste. The paste was mixed with 15% and 25% cefadroxil and gelatin, then cast into pellet molds for drug administration.

Dissolution experiments

Dissolution tests were conducted at 37ºC using a six-paddle dissolution tester at 100 rpm. To stimulate the gastrointestinal tract (GIT), 900 cc of phosphate buffer solution (pH 5.8 and 7.4) was dissolved. Every time, a 5 ml aliquot was utilized to analyze cefadroxil at a defined time. Stock solution was added to dissolving media. The quantity of cefadroxil emitted was measured at 230 nm using a UV spectrophotometer.

Characterization was done with XRD.

IV. RESULTS AND DISCUSSION

X-ray diffraction studies

By using solution intercalation, X-ray diffraction was able to discern the structure and apparent interlayer spacing (d spacing) of SPI/MMT nanocomposites. Figure 1 displays the XRD patterns of the nanocomposites and MMT. Based on a diffraction peak at $2\theta = 6.4$, the Bragg function was used to determine that the basal spacing of pure MMT is 1.4 nm. Soy protein does not have an ordered structure in the 2θ range of 1 to 10ºC, since the MMT free since-01 does not display a diffraction peak at this temperature. When the MMT concentration for AS-03 approaches 2.5 wt%, the X-ray diffraction spectrum does not show the diffraction peak of the MMT tactoids. This data points to a very disordered state of the MMT layers inside the nanocomposite powders. The XRD patterns show an intercalated structure with d-spacing values of around 3.0 and 2.6 nm for AS-04 and AS-05 powders, respectively, as revealed by the diffraction peaks. above low MMT contents, soy protein macromolecules delaminate the layered MMT in the aqueous medium; above 7.5 wt% MMT level, the intercalated structure of MMT in soy protein matrices becomes dominant.

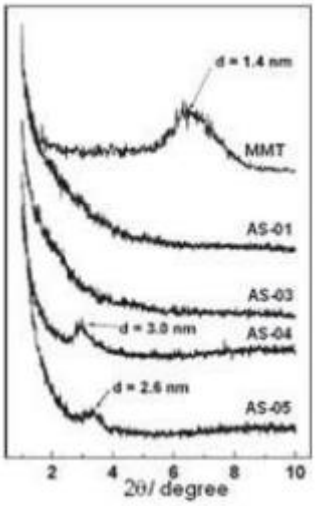

Figure 1:Structural Characterization of SPI–Furfural Nanocomposites by XRD

In-vitro drug release

The goal of developing the drug delivery system was to ensure that the medications could be brought up, retained, released, activated, localized, and targeted at the correct time, dosage, and location. By imbuing the medications with its unique properties, the biodegradable polymer can make a significant contribution to this technology. Here, biodegradable polymers like PLA and PCL are popular choices because they are easy to work with in mild environments, mimic the body's natural rigidity, and are biodegradable and crystallinity-free, making them suitable for usage with a wide variety of drugs. Films, gels, microcapsules, microspheres, nanoparticles, polymeric micelles, and polymer-linked pharmaceuticals are among the formulations available for drug delivery systems.

Binding the medication to the polymer by physical interactions is often favored since it does not disrupt the molecular structure of the drug, unless doing so would result in the loss of bioactivity. A nanocomposite of soy protein isolate and furfural has been combined with the hydrophilic medication cefadroxil. Because of its low cost, biodegradability, lack of toxicity, and abundance of pendant groups like OH, SH, and NH2 that may be attached to drugs to create polymer-drug conjugates, soy protein is an attractive option for drug delivery systems (Fig. 2). Conjugate formation may be facilitated by weak hydrogen bonding between the carboxyl group of the drug and the hydroxyl group of the soy protein isolate.

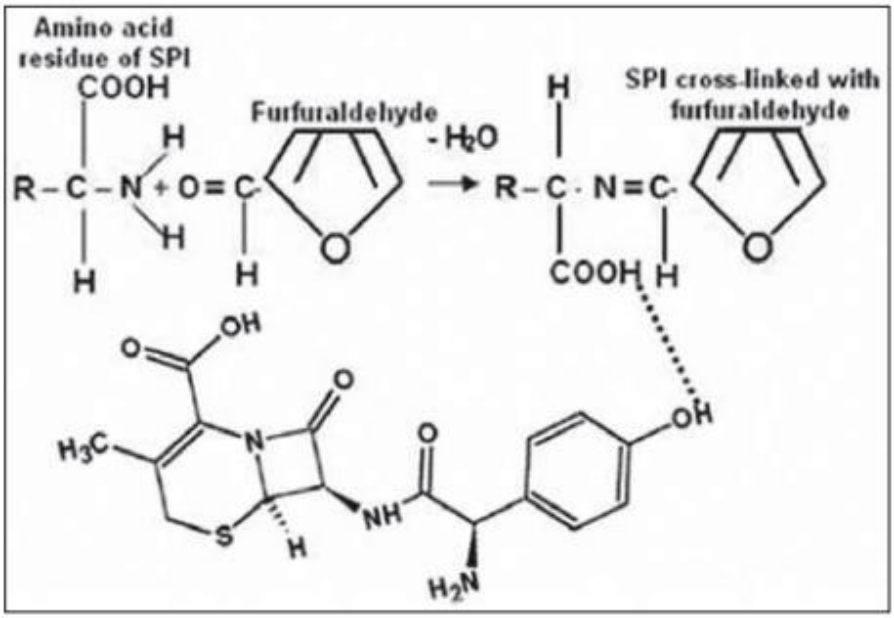

Figure 2:Proposed Mechanism of Polymer–Drug Conjugate Formation

A new nanoparticle formulation utilizing cefadroxil as the medicine is being developed in this study. It consists of biodegradable soy protein cross-linked with furfural and medicinal clay MMT. Biological half-life for a dosage containing 0.5 to 1.0 gram of the antibacterial medication cefadroxil is 1.2 hours. The process of chemically attaching the side chain (D)-p-hydroxy phenyl glycine to β-lactam results in cefadroxil. For those who are interested, cephalosporin antibiotics are a common choice for fighting against germs.

For nanoparticles to be able to pass the GI (gastrointestinal) barrier, MMT can provide them mucoadhesive capabilities 43. The structural family to which MMT belongs is 2:1 phyllosilicate, and it is also a powerful detoxifier. Dietary toxins, bacterial toxins linked to gastrointestinal disruption, hydrogen ions in acidosis, and metabolic toxins including steroidal metabolites linked to pregnancy are all things that MMT might potentially absorb. The medicinal clay rapidly eliminates any harmful substances that generate negative radiations because it is irresistibly drawn to them.

Research on the in-vitro drug release using a 10% furfural/5% organoclay formulation has been conducted at acidic, neutral, and alkaline pH levels, with drug loadings of 15% and 25%. In Fig. 3 and 4, we can see the percent cumulative release plotted against time for various pH types. Reviewing the data, one may deduce that the drug release is sensitive to both the medium's pH and the kind of polymer matrix. To illustrate the point, when

cefadroxil is loaded at 15% (Fig. 3), 96% of the antibiotic is released at 15 hours when the pH is 7.4, but only 85% when the pH is 5.8.

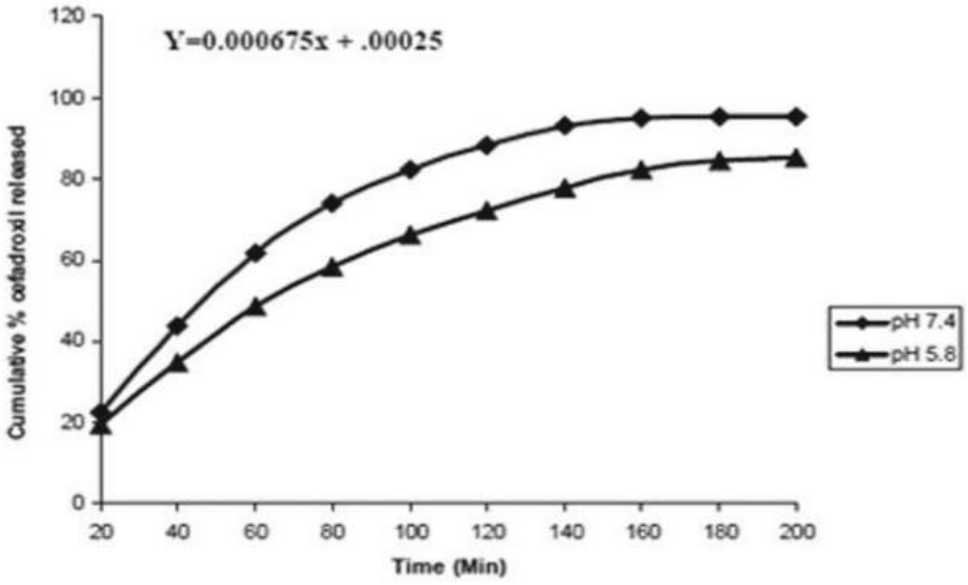

Figure 3:Effect of pH on Cumulative Cefadroxil Release (15% Drug Loading)

At 15 hours, the cumulative drug release percentage is 98 at pH 7.4 and 91 at pH 5.8 for a 25% drug loading scenario (Fig. 4). This is because the drug's cumulative release is accelerated in an alkaline environment, where the hydrogen connection between the two moieties breaks broken. Increases in drug loading from 15% to 25% are accompanied with an increase in the cumulative release rate from 96% to 98%.

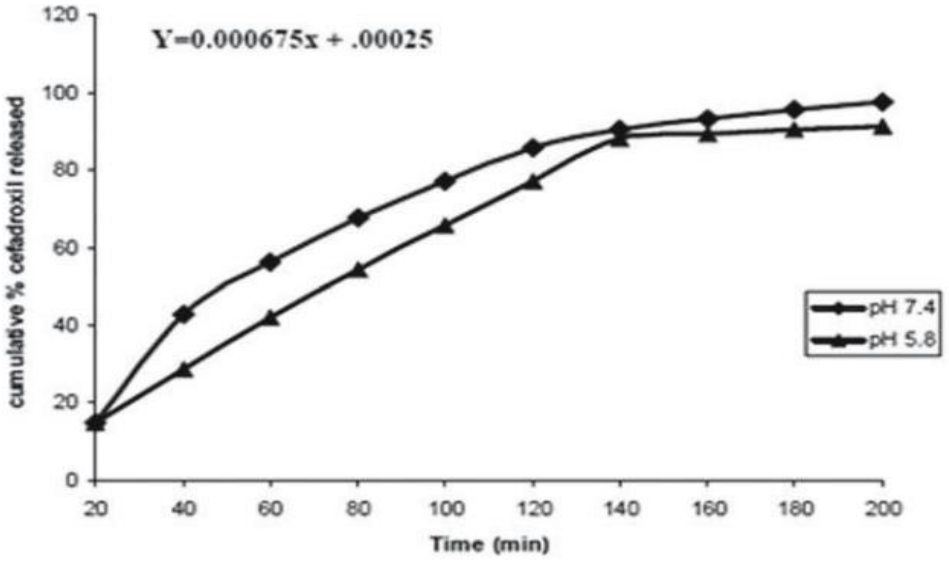

Figure 4:Effect of pH on Cumulative Cefadroxil Release (25% Drug Loading)

Drug release kinetics

To determine the kinetics of drug release, we fitted the cumulative release data to a single exponential equation and plotted the results against time.

$M_t / M_\infty = kt^n$

Where M_t/M_∞denote the fractional release of the drug at time t, where k is a constant property of the drug polymer system and n is an empirical value that describes the release process. We used the data in Table 1 and the least squares method to calculate the values of n and k at various pH levels.

Table 1:Drug Release Kinetics Parameters of SPI–Furfural–MMT Nanocomposites

%Drug Loading	pH	n	K
15%	7.4	0.70	0.18
	5.8	0.68	0.12
25%	7.4	0.66	0.27
	5.8	0.59	0.12

Assuming n = 0.5, the medication diffuses through the polymer matrix and is released according to the Fickian diffusion process. When n > 0.5, drug diffusion of an abnormal or non-Fickian kind happens. A kinetics that is entirely non-Fickian is at work when n = 1. In this investigation, an unusual form of diffusion transport is indicated by n values that are more than 0.5 but less than 1. It is clear from comparing the k-values that the rate constant is greater in acidic pH than in alkaline pH, which is in agreement with the release rate.

V. CONCLUSION

An efficient biodegradable carrier for regulated drug administration may be found in soy protein isolate-furfural nanocomposites reinforced with montmorillonite clay, as demonstrated in the present work. According to XRD examination, the structural organization of the nanocomposites was affected by the clay content; lower clay concentrations encouraged MMT delamination inside the protein matrix, whereas higher clay

levels supported the creation of intercalated structures. Cefadroxil in vitro drug release studies showed that drug loading, medium pH, and polymer-clay interaction type significantly impacted release behavior. The medication diffuses more quickly in an alkaline environment because hydrogen bonding inside the matrix is weaker, as seen by the higher cumulative release at pH 7.4 compared to pH 5.8. A combination of diffusion and polymer relaxation was shown to be the mechanism of drug release by kinetic modeling, which revealed that it followed anomalous (non-Fickian) transport.

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