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Obtaining the palygorskite:chitosan composite for modified release of 5-aminosalicylic acid

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ABSTRACT

This study's aim was to obtain composites from palygorskite (PLG) and chitosan (CS) in order to modify 5-aminosalicylic (5-ASA) release. Initially, the PLG:CS composite was obtained using glutaraldehyde (GLA) as a reticular agent. Then, PLG, CS and PLG:CS were characterized by means of analytical techniques such as CHN elemental analysis, surface area analysis, XRD, FTIR, DSC and TG, SEM, adsorption tests and release profiles. Based on analytical data, the formation of the PLG:CS composite which showed the presence about 19% of CS, decrease in specific surface area, morphological analysis modified, visible change of crystallinity, of FTIR and thermal analysis. In relation to the drug-composite interaction, PLG:CS exhibited a significant increase in adsorption with 5-ASA at 58.24% in relation to PLG and CS which were at 16.29% and 23.96% respectively. The release profiles show that the PLG:CS composite changed the 5-ASA release speed in analyzed simulated fluids (intestinal and stomach) unlike other systems. Thus, the PLG:CS composite with proven synergy of the PLG and CS inherent properties showing 5-ASA effective modified release. Hence, this composite has potential benefits for the vectorization of drugs.

1. Introduction

Composites materials consisting of inorganic and organic parts have attracted attention due to their numerous practical applications in the biotechnological fields such as enzyme immobilization, chromatographic area, clarification of oils, paints, cosmetics and pharmaceuticals. The development of composites, formed from polymers and clay, have been an alternative to conventional filling of polymers, due to clay's ability to form dispersions at the nanoscale, improving significantly the mechanical and physical properties when compared to polymeric composites on a microscale. Some studies have continued to report the improvement of chitosan/clay thermal barrier properties and water solubility leading to significant industrial development which can be used in medical and biomedical applications [1–4]

The majority of polysaccharides are usually found neutral or negatively charged in acid environment except chitosan (CS). CS is a copolymer of d-glucosamine and *N*-acetyl-D-glucosamine obtained from chitin deacetylation. When in acid solution, the amino groups (—NH_2) of the glucosamine are protonated to —NH_3^+, suitable to interact with anionic groups that modify its physicochemical characteristics [5,6].

Due to high solubility in an acidic medium (pH < 2), CS alone is incapable of preventing the release of drugs in their pharmaceutical forms during their passage through the stomach and the small intestine. To avoid this problem, pH-dependent coatings, reticulation frequently with glutaraldehyde (GLA) and the insertion of other polymers have been studied [7,8].

When reticulated, CS possesses greater mechanical strength and is more applicable in biochemical engineering but there are also operating defects such as granule density that is very similar to that of water (which leads to easy flotation) and its texture is not so rigid. The problems mentioned can be improved in conjunction with other powders, such as clay and activated charcoal, to increase density and enhance mechanical strength, and, thus, extend their applications [8].

Non-lamellar clays, such as palygorskite (PLG), are being used for the preparation of biocomposites that provide relevant properties due to their unique morphology and surface characteristics that increase the behavior of the mechanical properties associated with their fibrous structure in addition to favoring complexation with biopolymers through hydrogen bonds by means of silanol (Si—OH) groups on the clay [9] surface.

Due to benefits achieved, composites derived from PLG and CS can be used for the release of colon-specific medications such as 5-aminosalicylic acid (5-ASA). This is because CS is biodegradable in the

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Table 1
Analysis of S_{BET} (specific surface area), S_{ext} (external surface area) e V_{total} (total pore volume) of PLG and PLG:CS.

Materials	S_{BET} ($m^2 \cdot g^{-1}$)	S_{ext} ($m^2 \cdot g^{-1}$)	V_{total} ($cm^3 \cdot g^{-1}$)
PLG	118.04	146.71	0.34
PLG:CS	56.03	94.02	0.14

Table 2
Elemental analysis of carbon (C), hydrogen (H) and nitrogen (N) contained in the materials CS and PLG:CS.

Material	% C	% H	% N	C ($mmol \cdot g^{-1}$)	H ($mmol \cdot g^{-1}$)	N ($mmol \cdot g^{-1}$)
CS	38.98	7.00	6.73	32.48	70.00	4.80
PLG:CS	36.87	5.71	1.76	30.73	57.10	1.26

presence of specific colon enzymes and PLG would function in the control of this degradability starting from the interaction between these two materials thereby resulting in the release of the adsorbed drug [7].

On the basis of the above, this research aimed at obtaining and characterizing composites starting with PLG and CS and used the reticular agent GLA for the modified release of 5-ASA.

2. Materials and methods

2.1. Material

Chitosan (CS) powder was acquired by Polymar with a deacetylation degree of 86.2%, molecular mass of 50,000 Da and its viscosity is 50 cPs at 20 °C. Palygorskite (PLG) was acquired by Mineração Coimbra Ltda, Guadalupe-PI (Brasil). 5-aminosalicilic acid (5-ASA) was purchased from Phamanostra. Glutaraldehyde (GLA) 50 wt%, sodium hypochlorite, hydrogen peroxide (35%), acetic acid glacial used were of analytical grade.

2.2. Preparation of CS

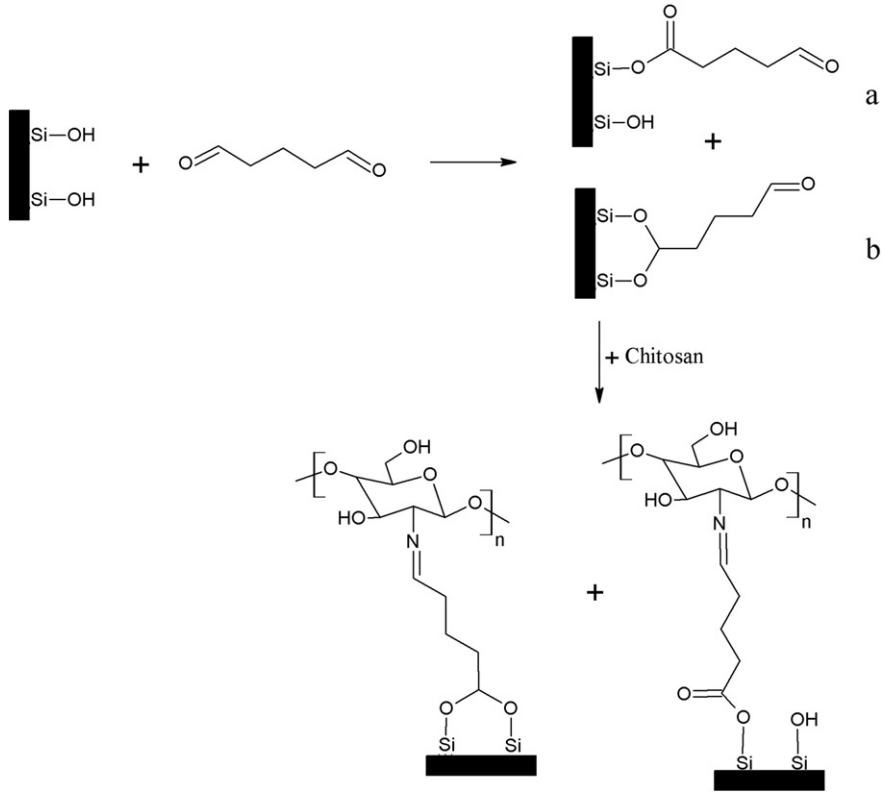
CS suspension was prepared with purified water and sodium hypochlorite 3.6% was added, for reducing shrimp's characteristic odor, under magnetic stirring for 1 h [10]. Then CS was isolated by centrifugation at 3000 rpm for 5 min, washed and dried at 80 °C for 4 h.

2.3. Treatment of PLG

200 g PLG *in natura* was washed with purified water and dried for two days at 30 °C. PLG was dispersed 400 mL of sodium acetate buffer solution pH 5.0 ± 0.5, under magnetic stirring until temperature stabilization at 50 °C, to carbonates decomposition. Then, 120 mL of hydrogen peroxide 35% was added in other to withdraw organic materials inside pores. The system was maintained as long as any reaction (foaming) was observed [11]. PLG suspension was isolated by centrifugation at 3000 rpm for 5 min, washed with purified water, dried and sieved at 200 mesh.

2.4. Obtainment of PLG:CS

Material PLG:CS was prepared according to PENG et al. [12] with adaptations, by adding of 2.0 g PLG soaked into 7.5 mL GLA (25 wt%) and it was added purified water to a final volume of 30 mL, under stirring for 4 h. 2.0 g of CS powder was dissolved in 100 mL acetic acid solution (1 wt%) using a magnetic stirrer at room temperature for 4 h and pH adjusted to 5.0 ± 0.2 with NaOH 1 M. CS solution was added slowly to PLG suspension/GLA and the mixture was mixed with magnetic stirrer for 3 h at 30 °C. The pH was maintained throughout the reaction. After, the pH was elevated to 11.0 ± 0.5 for an hour to enhance crosslinking and adsorption of CS on PLG once in basic pH the clay have greater anionic force increasing of CS amount to necessary to equalize the clay charge. Then, the material was isolated by centrifugation at 4000 rpm for 5 min, washed, dried and sieved at 200 mesh.



Scheme 1. Proposed interaction between materials palygorskite and chitosan from insertion of cross-linked glutaraldehyde.