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Preparation and characterization of cellulose derived from rice husk for drug delivery

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ABSTRACT

Cellulose has been the extracted from rice husk by chemical treatment with aqueous solution of sodium hydroxide. The physical properties of derived cellulose (water uptake and swelling behavior) has been investigated with view of different applications. The morphology and chemical structure were investigated by Infrared spectroscopy (FT-IR), Scanning electron microscopy (SEM) and Thermogravimetry (TG) techniques. The results revealed the formation of homogeneous porous (micro size) membrane. Further, the UV-vis spectra of cellulose in different pH shows its responsiveness towards hydronium ion, which is suitable for drug delivery. Further, obtained cellulose was used for drug delivery under optimized pH.

Keywords: Rice husks; cellulose; pH responsiveness; drug delivery.

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Introduction

In recent years, the agro waste materials has created intensive research interest of scientists to use in technology development due rich content and poor waste management technology **[1-2]**. One of the potential agro-wastes is rice husk (RH), which is available in large quantity as a waste from rice milling industries. The composition of RH is 35% cellulose, 25% hemicellulose, 20% lignin and 17% ash (mainly 94% silica by weight) **[3-4]**. The collection and disposal of RH is difficult and thus generally left unused or simply burnt as a crude source of energy **[5-7]**. The advantageous feature of RH is renewable nature, low density, and nonabrasive with reasonable strength and stiffness. In responding to the needs of environmentally friendly composites, efforts are being made to produce RH composites with different polymers such as poly(lactic acid), poly butylene succinate (PBS), Polypropylene(PP) **[8]**. These composites have been used in automobile industry, building profile, decking and railing products **[9]**. However, the basic constituents of RH is cellulose, a thermodynamically stable, crystalline structure with numerous hydrogen bonds. The chemically modification of Cellulose on alcoholic sites has been explored for various application **[10-11]**. The cellulose derivatives are also recommended for different biomedical applications such as drug delivery and tissue engineering **[12]**. Chemical modification of cellulose functionalizes different position (e.g., oxidized, esterified, alkylated at hydroxyl group) to generate specific solubility. The oxidized cellulose called oxycellulose is an important biocompatible and bioresorbable polymer, which is widely used in medical applications. The cellulose based materials can be easily sterilized, bears unique properties like excellent biocompatibility and antioxidant activity thus used to control wound and organ transplants **[13-15]**. Eethyl cellulose and methyl cellulose have been used for drug delivery because its complexing properties with bioactive agents **[16]**. The cellulose also reduces the toxicity on drug and increases their efficiency **[17]**. The present paper reports the optimized extraction condition of cellulose from RH. The various properties like morphology, structure and responsiveness has been studied. Further, obtained cellulose was explored for use in drug delivery.

Experimental

Materials and methods

Rice husk was obtained from Kundan Rice Mill, India whereas sodium hydroxide 99.9% was procured from E. Merck, Germany and use without further purifications.

Isolation of cellulose and casting of membrane

Rice husk was grinded with 50 ms size in a grinder, the grinded rice husk washed with distilled water and dried at 100 ^{O}C. Further, 20 g of rice husk was treated with 20 ml 10% NaOH aqueous solution and 80 ml distilled water with stirring on a magnetic stirrer for half an hour at constant temperature (60 ^{O}C). The obtained slurry was filtered and liquid part consist of cellulose, washed with distilled water and then neutralized by adding 1N HCl drop by drop. The obtained solution was spin casted at 500 rpm to make a film with thickness of film was 0.025 cm on a glass slide after drying in a vacuum oven at 60 ^{O}C.

Characterization

FT-IR spectra was recorded on Bruker (alpha) FT-IR spectrometer by making pellet with dehydrated KBr at 10 ton pressure. ZEISS, model MA-15, Scanning Electron Microscope have been used to study surface morphology. However the DTG-60, Shimadzu Corporation Japan thermal analyzer was used for taking thermogram at heating rate 5 ^{O}C per minute in 100 ml N_2 gas flow.

Swelling study

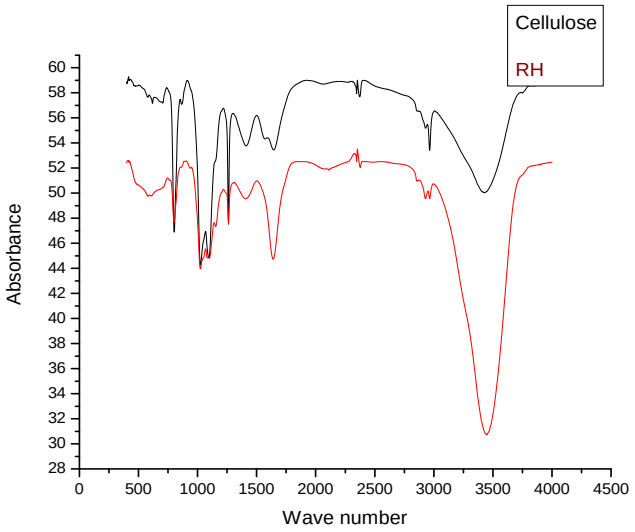
The prepared films were peeled out and cut into 1 x 1 cm^2 samples, then dried at 100 ^{O}C for a period of 6 h to remove the moisture content. The dry weight of each sample was noted initially and immersed in 0.1 M solutions of NaOH. After a fixed time interval (5 min), the samples were taken out, wiped carefully with filter paper. Then thickness and mass were measured by screw guage and digital electronic balance (shimadzu corporation japan, least count 0.05 mg). The weights and thickness were measured in triplicate and their mean was reported. Further, the percentage weight gains were calculated by equation (1) and welling by difference in thickness.

$$W = \frac{M_w - M_d}{M_w} X100 \quad (1)$$

where M_w and M_d are wet and dry mass of film. The thickness was calculated by difference of dry and soaked film. The observed percentage weight gain and swelling were found to be 118.27% and 21.2%, respectively.

Responsive nature and in vitro drug delivery

The UV-Vis spectra of prepared cellulose was measured as such and after treating with vapor of HCl to check responsive nature by UV-3600, Shimadzu, UV-Vis spectrophotometer, The drug release rate has been measured for a medicine (shelcal-500 Elder Elder Pharmaceuticals Pvt. Ltd, contains calcium carbonate a nutritional supplement of calcium) by monitoring dissolution of medicine at different time interval. For, this purpose square piece (1 x 1 x 0.05 cm) of cellulose membrane has been soaked in 2000 ppm aq. solution of shelcal for 5 min and then taken out. The surface was wiped out with alcohol soaked tissue paper and the dried in room temperature for 1 h (room temperature @ 32 ^{O}C) and square pellet like structure was found. Further, the pellet was kept in two beaker containing 100 ml water at different pH maintained by appropriate buffer tablet. While in one beaker the same weight of shelcal tablet was kept in 100 mL water for reference dissolution pattern. One ml water from each beaker was taken out at the interval of 5 minute and concentration was measured by comparing absorbance of solution recorded by a colorimeter at wave length 620 nm.



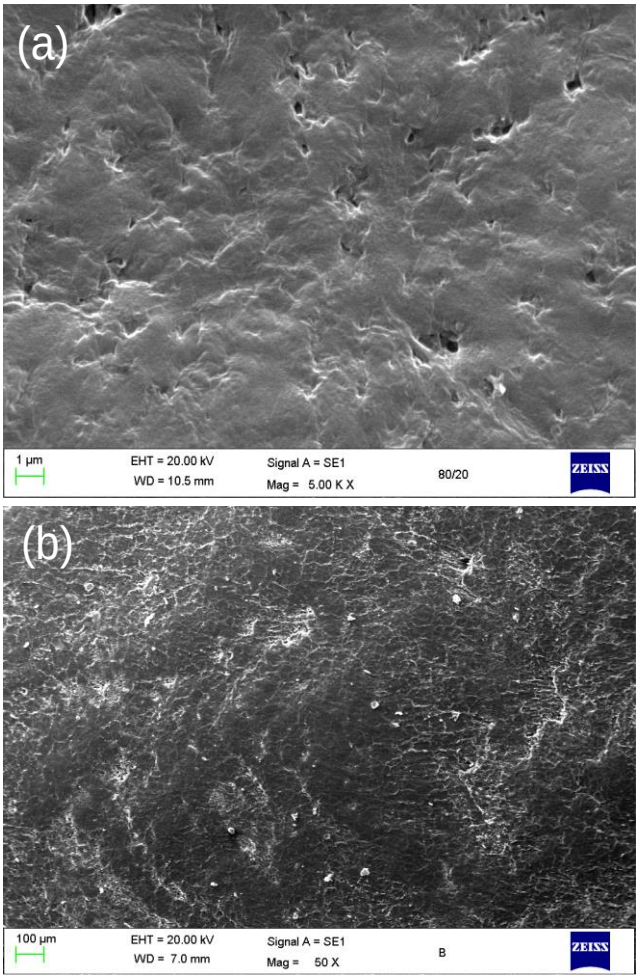


Fig. 2. SEM micrographs of (a) RH and (b) separated cellulose.

Results and discussion

Separation and chemical characterizations

The alkali treatment of RH makes cellulose soluble due to the formation of sodium salt **[18]** and separated from other constituents. Further the acid neutralization regenerate the insoluble cellulose with modified structure because of re-solidification process of pure cellulose. The overall scheme is given in equation (2):

$$\text{Cellulose} \xrightarrow{\text{NaOH}} \text{Cellulose--Na} \xrightarrow{\text{HCl}} \text{Cellulose} + \text{NaCl} \text{ ---1} \qquad (2)$$

Fig. 1. FTIR spectra of RH and separated cellulose.

The polymers are having both crystalline and amorphous nature, their proportionality is important for processibility, optical, mechanical and chemical properties. FTIR spectra of RH and cellulose are shown in **Fig. 1**. The FTIR spectra of cellulose are showing peaks at 813 for C-O-C (β1→4) band due to amorphous nature and at 1415 for CH_2 due to crystalline nature **[19]**. The intensity of amorphous band is sharply increased in cellulose than RH, indicates increment in amorphous nature in isolated cellulose. It supports better the utility of isolated cellulose in casting or film forming abilities. The other characteristics IR peaks of cellulose are at 2854 cm^{-1} (CH_2), 1090 cm^{-1} (pyranose ring) and 1265 cm^{-1} (C-O-C aryl-alkyl) and 1645 cm^{-1} (adsorbed water). The FTIR peaks appeared at 592 cm^{-1} in RH is due to presence of silica is disappeared in cellulose spectra indicates the removal of silica present in rice husk. However, IR peak at 3432 cm^{-1} in RH for hydrogen bonding is showing considerable shift in RH due to reaction with alkalis, which may be due to hydrolysis **[20]**.

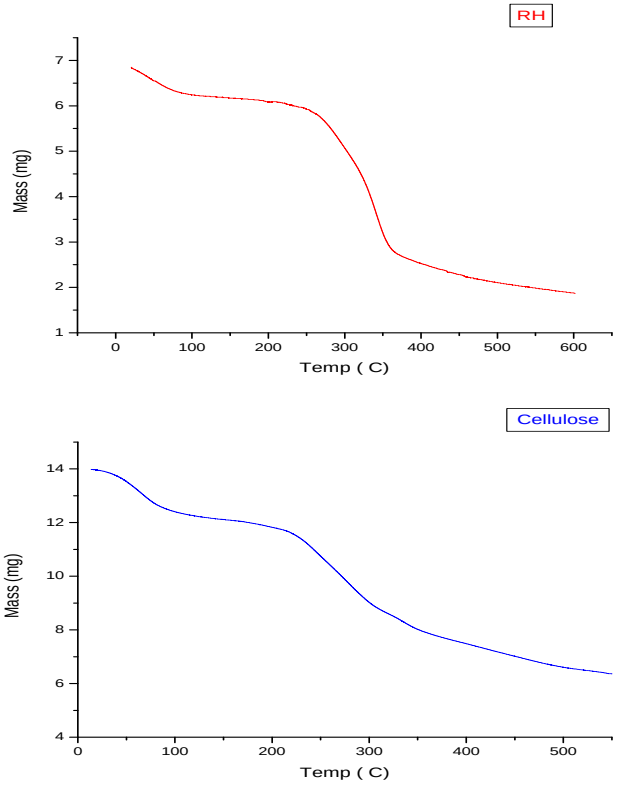


Fig. 3. TG curve of RH and Cellulose.

The morphology of obtained cellulose and RH is shown in **Fig. 2 (a** and **b)**. The micrograph clearly indicates the porous, non-planner nature of obtained cellulose. TG

curve of RH and cellulose is shown in **Fig. 3**. TG curve of derived cellulose from rice husk is showing weight loss in two steps initially 13% below 133 ^{O}C due of removal water molecules followed decomposition between 200 to 560 ^{O}C with weight loss of 42%. However, RH is showing weight loss 9% below 133 ^{O}C associated with sharp decomposition till 400 ^{O}C with a weight loss 51%. It indicates the chemical treatment softens the matrix along with formation of some sort of linkage between different molecules after removal of silica.

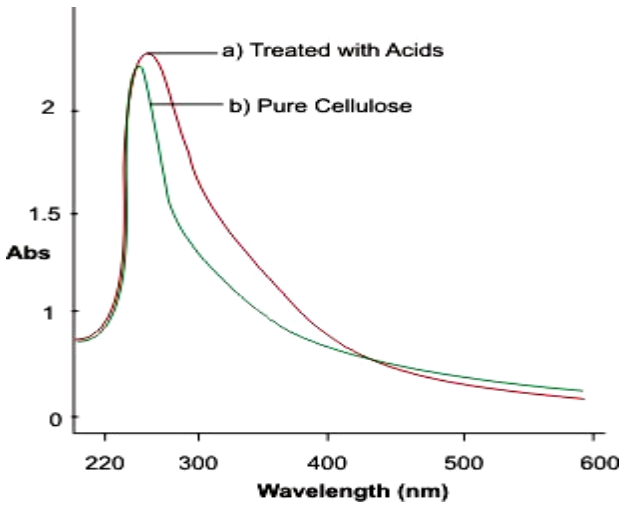


Fig. 4. UV spectra of pure and acid treated cellulose.

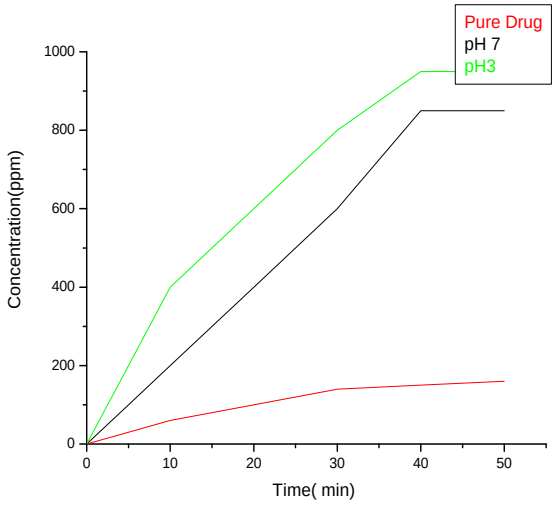


Fig. 5. Trend of drug release in different conditions.

pH responsive nature and in vitro drug delivery

Chemically, cellulose is a linear homopolymer of glucose consisting of D-anhydroglucopyranose units linked by glycosidic bonds. Being a homopolymer of glucose, cellulose is not water soluble, crystalline in nature because of extensive intra and inter-molecular hydrogen bonding. The disruption of this hydrogen bonding either by chemical modification to the cellulosic backbone or by the use of suitable solvents can modify cellulose or produce cellulose derivative at large scale. The chemical modification also makes it water dispersible cellulose, an important material in biomedical applications and many efforts have been made **[21]**. The UV curve of cellulose as such and after treated with 0.1N HCl is sown in **Fig. 4**.

Table 1. Drug release profiles.

Time (min)	Pure drug (ppm)	Drug loaded in cellulose (ppm)	
		pH (7.4)	pH (3)
0	0	0	0
5	100	30	250
10	200	60	500
20	400	100	800
30	600	140	950
40	850	150	950
50	900	160	950

The graph indicates the shift in λ max due to some sorts of change in cellulose with acid treatment. Such types of materials are reported as suitable for different biomedical application like drug carrier. Here, we feel that alkali treatment of cellulose hydrolyses its network and makes many free group in chain, which are not free in natural state. Further, when it is exposed hydronium ion it oxidizes partially and causes shifting in peak maxima of UV spectra. This may also causes the dissociation on hydrogen bonding in acidic pH, an important criteria for drug delivery at defined sites. There are three reaction methods to control release of drug molecule: erosion, diffusion and swelling followed by diffusion **[22-25]**. The release rate of shelcal at different pH (neutral and 3.0 pH) for pure drug and drug soaked in cellulose film is shown in **Fig. 5** and **Table 1**.

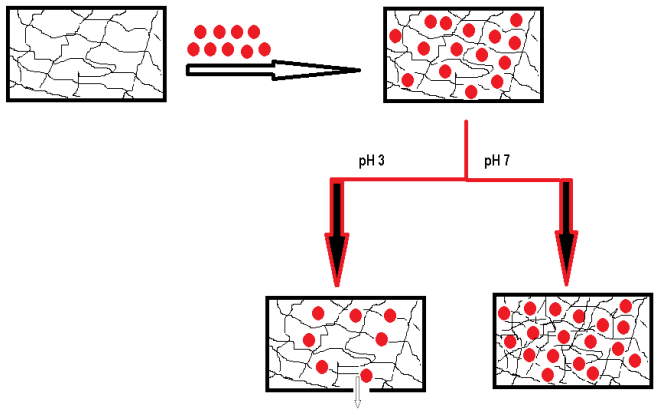


Fig. 6. Illustration of drug release in different pH.

The data reveals that alkali treatment of cellulose modifies the release effect of shelcal **[26]**. The release in neutral pH with cellulose is slow than pure drug but in acidic media the release rate in cellulose soaked medicine is faster than pure drug. However, the trend in the case shelcal

soaked in cellulose is showing very small release due to binding behavior of cellulose with divalent Ca^{+2} cations **[16]**. However, the increment in acid behavior polymer matrix swells and facilitates the release of drugs due dissociation of inter linking of chain. On the basis of above data an expected role of polymer chain is presented in **Fig. 6**. It indicates that cellulose combines with calcium ion of medicine and it form a network. The increase in hydronium ion dissociates (disrupts) bonding between hydroxyl group of cellulose and calcium ion of medicine releases sharply. However the increase in hydroxyl group does not supports the dissociation since it releases hydroxyl group due to common ion effect and reduces the rate of release.

The burst of polymer matrix followed by controlled drug release from the cellulose carrier showed that the release obeys a diffusion-controlled mechanism; however, the diffusion rates at each stage of the drug release differed considerably, suggesting that two different processes may be taking place. On comparing pH responsive data, it is concluded that at tow pH the hydrogen bonding network of cellulose degraded and thus matrix becomes loose and hence it supports the rapid release in specific organ. The trend in release indicates the simple model is being followed by equation (3):

$$D \rightarrow \langle Body(X_t) \rangle \rightarrow Kc \tag{3}$$

Where, D is original amount, Xt is amount of drug deposited, Kc is drug release rate. The presence hydroxyl group in cellulose supports the gelation effect with calcium ion and creating binding network. The gelation effect increases the activation energy and it need to be additional energy like heat, chemical etc. to degrade. In this case the in increment in pH ion is responsible to change the activation energy and supports the degradation as well as pH controlled drug delivery and followed kinetics as equation (4):

$$X_t = X_0 e^{-(k)t} \tag{4}$$

The optimization of activation energy by creating polymeric network is an important criteria of drug designing. The biopolymer may functionalize by various methods like microwave assisted grafting, creating network by gelation can control the drug release in different form like oral, trans-dermal etc. Therefore the reported strategy opens the new dimension of bio-resource management as well as the modification chemically obtained cellulose for different biomedical application. The extracted cellulose is porous in nature therefore, it also supports for better gas exchange through it and also used for wound healing purpose.

Conclusion

Biologically active cellulose has been isolated from a rice husk (an agro-waste) by chemical treatment with sodium hydroxide. The obtained cellulose was characterized and found porous in nature as well as chemical responsive towards hydronium ion, which is suitable for different biomedical applications. The effect of binding behavior of cellulose with shelcal has been studied for bio-resource management. The composite cellulose and shelcal was studied for drug release profile by measuring the liberated calcium content. The role of sheathing the drug by cellulose has been explained along with kinetic model to explain the drug release.

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