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Physicochemical And Pharmaceutical Evaluation Of Cellulose And Na-CMC Obtained From Bagasse And Leaves Of Sugarcane Species Co-7527

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Abstract:
This study explores the sustainable valorisation of agro-industrial waste by extracting cellulose and synthesizing sodium carboxymethylcellulose (Na-CMC) from the bagasse and leaves of sugarcane (variety Co-7527). The objective was to comprehensively evaluate these polymers for their potential as pharmaceutical excipients based on physicochemical properties, performance in solid dosage forms, and economic feasibility. The extracted celluloses and their Na-CMC derivatives underwent rigorous analysis, including assessments of solubility, assay value, metallic impurities, starch contamination, water retention, and swellability.

Results indicated that while cellulose and Na-CMC from leaves exhibited superior overall physicochemical characteristics, the derivatives sourced from bagasse demonstrated enhanced stability profiles. A key finding was the significantly superior water retention and swellability capacity of the bagasse-derived Na-CMC (C1/CMC1) compared to the leaves-based product (C2/CMC2). Critical quality attributes for polymers were confirmed; the degree of substitution for both synthesized Na-CMC samples exceeded the pharmacopeial threshold of 0.4, and the degree of polymerization was higher for bagasse-derived cellulose (830) than for leaves-derived cellulose (654). Pharmaceutical application tests in model solid dosage forms confirmed the functional suitability of both Na-CMC types as effective excipients.

A preliminary pharmacoeconomic assessment confirmed that deriving these polymers from sugarcane waste is highly cost-effective. This work concludes that bagasse and leaves from sugarcane Co-7527 are viable and sustainable sources for producing high-quality cellulose and Na-CMC. This approach not only provides a low-cost alternative for the pharmaceutical industry but also offers a lucrative waste management solution, enhancing the overall economic viability of sugarcane cultivation and supporting circular bioeconomy principles.

Keywords: Sugarcane bagasse; Sugarcane leaves; Cellulose extraction; Sodium carboxymethylcellulose (Na-CMC); Pharmaceutical excipient; Waste valorization; Pharmacoeconomics; Biopolymer.

1. Introduction

Cellulose, a naturally abundant biopolymer, is a fundamental structural component of plant cell walls, typically found alongside lignin, hemicellulose, pectins, and waxes. Traditional commercial sources, such as wood pulp and cotton, have driven significant deforestation, highlighting an urgent need for sustainable alternatives. Consequently, current research is increasingly focused on identifying novel, non-conventional cellulose sources and developing environmentally benign methods for deriving valuable cellulose esters and ethers (Van de Vyver et al., 2011; Rutkowski, 2011).

Sugarcane (*Saccharum officinarum* L.) generates substantial lignocellulosic waste in the form of bagasse and leaves, presenting a promising and underutilized resource. Bagasse consists of approximately 43.68% cellulose, while leaves contain 35–40.84% (Luz et al., 2007; Moutta et al., 2012). For every 10 tons of processed sugarcane, about 3 tons of bagasse are produced, which is often repurposed for energy generation or in commercial applications within the food and pharmaceutical sectors. In contrast, sugarcane leaves are frequently left in fields as fodder or burned, despite their significant cellulose content. Utilizing this waste for cellulose extraction aligns with circular economy principles and offers an additional revenue stream for the sugarcane industry. Sodium carboxymethylcellulose (Na-CMC), a key semi-synthetic cellulose ether, is widely used in pharmaceuticals, food, and textiles due to its excellent water solubility and functionality as a thickener, binder, and stabilizer (Barba et al., 2002). Global production exceeds 360,000 metric tons annually, typically synthesized via a two-step alkali-catalyzed reaction of cellulose with monochloroacetic acid (MCA) in an alcoholic medium (Dapia et al., 2003; Heinze et al., 2018). The degree of substitution (DS) is a critical parameter determining Na-CMC's application, with commercial grades generally ranging from 0.5 to 1.4 to ensure optimal solubility and performance.

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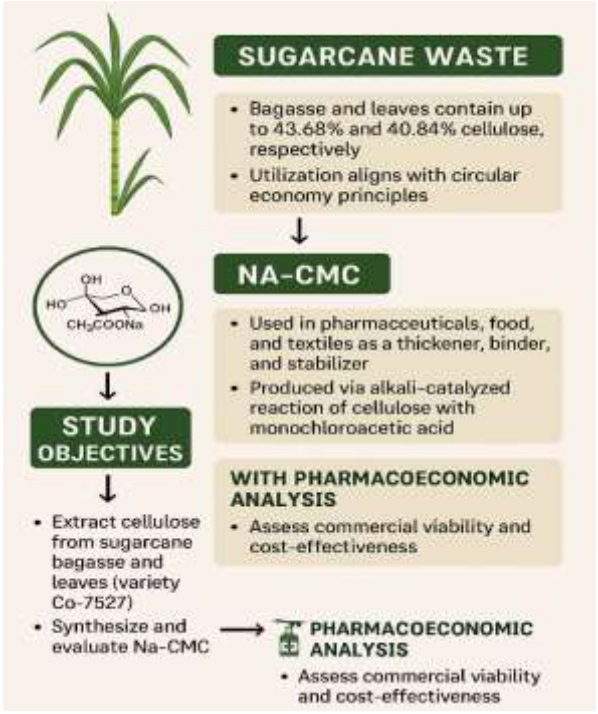

Figure 1 Transforming sugarcane waste into high-value Na-CMC supports circular economy goals.

Previous studies have successfully produced Na-CMC from various agricultural wastes, including banana pseudostem, durian rind, and cotton gin waste (Adinugraha & Marseno, 2005; Rachtanapun et al., 2012; Haleem et al., 2014). However, the potential of sugarcane leaves remains comparatively unexplored. This study aims to bridge this gap by extracting cellulose from sugarcane bagasse and leaves (variety Co-7527), synthesizing Na-CMC, and conducting a comprehensive evaluation of their physicochemical and pharmaceutical properties. Furthermore, a pharmacoeconomic analysis was conducted to assess the commercial viability and cost-effectiveness of utilizing these waste materials for producing high-value pharmaceutical excipients.

2. Experimental Section

2.1. Materials

All chemicals used were of analytical grade and procured from Sigma-Aldrich Co. (USA). Sugarcane bagasse and leaves (variety Co-7527) were obtained as waste products from Jain Farm, located on Kolhapur Road, Maharashtra State, India.

2.2. Methods

2.2.1. Extraction of Cellulose

Bagasse and sugarcane leaves were dried, ground, and sieved (mesh #20). The powder was autoclaved with distilled water at 121°C for 15 min, filtered, and dried. The material was then treated with 0.5 N NaOH for 2 hours, washed thoroughly with distilled water, filtered, and dried. A bleaching step followed using 6% sodium chlorite for 1 hour. The product was washed, dried, ground again, sieved (mesh #60), and stored in airtight polyethylene bags.

2.2.2. Synthesis and Purification of Na-CMC

Extracted cellulose was mercerized with NaOH in isopropanol for 1.5 hours. Monochloroacetic acid (MCA) in isopropanol was then added with continuous stirring, and the temperature was raised to 60°C for 3.5 hours. The resulting slurry was washed sequentially with methanol and ethanol, then dried to constant weight. Reaction parameters were optimized through iterative experiments, finalizing at 25% NaOH, 8% MCA, a temperature of 70°C, and reaction times of 1.5 hours for mercerization and 2.5 hours for etherification.

Purification involved dispersing the crude Na-CMC in distilled water, heating for 10 minutes, and centrifuging at 4000 rpm. The supernatant was precipitated in acetone, filtered, and dried at 60°C until a constant weight was achieved. The final product was ground and stored in moisture-proof packaging.

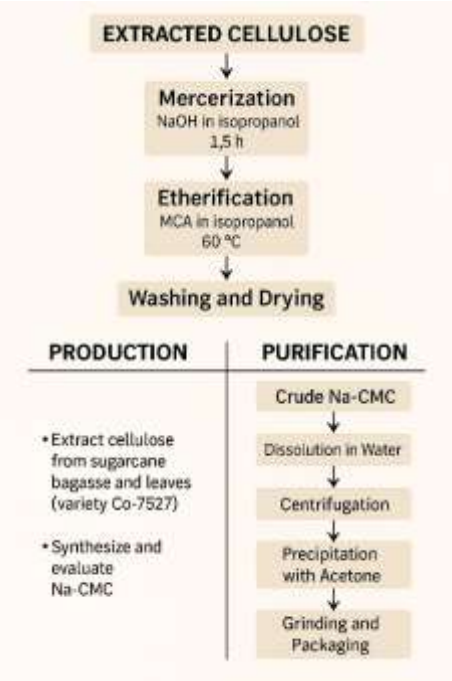

Figure 2: Stepwise synthesis and purification of Na-CMC from sugarcane cellulose, optimized for pharmaceutical-grade quality.

2.3. Analytics

2.3.1. Determination of Degree of Polymerization

The viscosity-average degree of polymerization (1DP) was determined using cupriethylenediamine (CED) as a solvent. Briefly, 0.25 g of dried cellulose was dissolved in 25 mL of 1M CED solution under a nitrogen atmosphere. The flow time of the solution was measured at 25°C using a Cannon-Fenske viscometer. The intrinsic viscosity was calculated and used to compute the DP according to standard methods.

Intrinsic viscosity was calculated (KV_1) of the powdered cellulose taken by the formula:

$$(KV_1) = t_1 (K_1) \qquad \text{(eq. 1A)}$$

in which K_1 was the viscometer constant.

Flow time t_2 for 0.5 M cupriethylenediamine hydroxide solution was determined by 100 cannon fenske or equivalent viscometer in seconds. The kinematic viscosity

$$(KV_2) = t_2 (K_2) \qquad \text{(eq. 1B)}$$

in which K_2 was viscometer constant.

The relative viscosity η_{rel} of powdered cellulose specimen was determined by the formula:

$$t_1 (K_1) = t_2 (K_2) \qquad \text{(eq. 1C)}$$

Intrinsic viscosity $(\eta)_c$ was determined by interpolation using the Intrinsic viscosity table in the reference table. The degree of polymerization P was determined as:

$$P = (95) (\eta)_c / Ws [(100- \% LOD)/100] \qquad \text{(eq. 4)}$$

in which Ws = weight in g of powdered cellulose taken and % LOD was taken from the test for loss on drying. The Degree of polymerization should be NLT 440 (USP monograph).

2.3.2. Substitution degree

Accurately weighing 5g, CMC was added to 200ml of HNO3: Methanol (1:1, v/v). After a few minutes of stirring, this solution was left for three hours. A 70% methanol solution was used to wash away the extra acid. Next, 200 ml of distilled water and 30 ml of a 1N NaOH mixture were used to dissolve 2g of the dried sample. 1N HCl was used to titrate the mixture. The following formulas were used to calculate the DS of CMC (ASTM, Toghrul, and Nurhan, 2013):
DS = (0.162*A)/ (1- (0.058*A)) (eq. 5A)

Equation 5B states that A= [(B*C) - (D*E)]/F
Whereas,
A: equivalent weight of alkali required per gram of sample;
B: amount of NaOH solution (ml);
C: normality of NaOH solution (N);
D: amount of HCl solution used (ml);
E: normality of HCl solution (ml);
F: weight of sample in (g)

2.3.3. Pharmacopoeial analysis of cellulose Various USP (USP29-NF24 page 3308) pharmacopoeial tests for powdered cellulose, such as water-soluble substances, starch, lead, pH, loss upon drying, and solubility. 2.3.4. Pharmacopoeial investigation of Na CMC USP monograph (USP29-NF34, Page no.338) tests were conducted, including the assay for sodium content, lead content, pH, foam test, precipitate test, color reaction, loss on drying, and sodium chloride.

2.3.5. The amount of swelling and water absorption
Fifty milliliters of water were combined with five grams of synthesized Na CMC. 1 cm-diameter films were made and then dried in a hot air oven. Weighing the sample's weight gain allowed us to check water uptake every five minutes. For both CMCs' films, the percentage swelling was computed.

2.3.6. Fourier transform infrared spectroscopy (FT-IR)
Infrared spectroscopy for cellulose and Na CMC from both sources was done from wavelength 4000-400 cm-1 in order to confirm group and its transitions using Bruker Spectrometer having model number ALPHA 100508 and Perkin Elmer model no. spectrum two having a serial no. 105627. This helps in understanding the characteristic nature of samples.

2.3.7. DSC, or differential scanning calorimetry
To learn how groups in samples behaved when exposed to heat, cellulose and Na CMC were heated to temperatures ranging from room temperature to 450°C. Understanding the relationship between temperature and sample degradation yields useful information about the sample's nature.

2.3.8. Diffractogram of X-rays
Samples were exposed to X-ray diffraction at an angle of 2Ɵ using Bruker AS's D8 Advanced, which produced data that clarified whether the sample was crystalline or amorphous. This ultimately aids in comprehending the sample's subsequent processing in its intended use.

2.3.9. SEM, or scanning electron microscopy
A scanning electron microscope (JEOL-JSM 6360A, Japan) was used to take photomicrographs of celluloses and Na CMCs at magnifications ranging from 1.0 kx to 10,000x. It makes it possible to determine the size, shape, and surface roughness of particles. Only carefully chosen photos are included here.

2.3.9. Zeta potential and particle size
The Horiba Scientific SZ-100 particle size and zeta potential analyzer has been used to analyze the particle size, polydispersity index, and zeta potential of all celluloses and Na CMCs.

2.4. Na CMC formulation
The tablet formulation of paracetamol contained 500 mg of paracetamol, 2.5% Na CMC, lactose (q.s.), and magnesium stearate (q.s.). The sodium CMC was synthesized from bagasse and sugarcane leaves. The weighed amount was taken and compressed right away.

2.4.1. Study of In-Vitro Dissolution
Both formulations containing synthetic CMC were subjected to an in vitro dissolution study using a Type-II dissolution test apparatus (Electrolab, TDT 08L, Mumbai, India) in accordance with the United States Pharmacopeia (USP). 900 milliliters of phosphate buffer were utilized as the dissolution medium, which was kept at 37.5 ± 0.50 degrees Celsius with a paddle speed of 50 rpm. Every sample was examined using UV visible spectroscopy with a wavelength maxima of 243 nm for pH 6.8.

2.4.2. Tests for disintegration, hardness, and friability
The Roche friabilator was used to check the friability in accordance with USP standards, using a standard speed of 25 rpm and 20 tablets. The Monsanto type hardness tester was used to test the hardness, and a standard disintegration test with a revolution of 75 rpm was carried out in the disintegration test apparatus using six tablets. Weighing the tablets

after testing allowed us to determine their friability. The weight loss of each tablet was then measured, and the mean was calculated. Pressure in kg/cm2 was used to measure hardness.

2.5. Pharmacoeconomics

The price of all raw materials was listed based on terms of negotiation for 1 ton by comparing costs with the prices of different distributors in order to determine the cost of C1, C2 (cellulose from bagasse and leaves) and CMC1, CMC2 (Na CMC from bagasse and leaves cellulose). Each step's components are listed based on the costing basis before being applied to the extraction price of 100 kg. This is just theoretical information derived from laboratory results and their application to large quantities. There may be some inaccuracies, so this comparison is made between the raw materials that have been used recently in the market—wood pulp and cotton linter—and the one made with bagasse and sugarcane leaves. Prices considered from various distributors for each raw material for reference are mentioned here. In pharmacoeconomics fixed prices which involve electricity, labor is not considered (Trask L., Pharmacoeconomics; Chapter 1: Principles, methods, and applications).

3. Findings and conversation

3.1. Reaction parameter results from CMC optimization

The degree of substitution began to rise immediately after the first step and increased as the steps were repeated. This indicates that viscosity was raised and carboxymethyl substitution was accomplished successfully.

3.2. The degree of polymerization and substitution

Understanding the substitution of carboxymethyl groups required an understanding of the degree of substitution. CMC1's degree of substitution fell between 0.4 and 0.85, while CMC2's degree of substitution fell between 0.4 and 0.73. Theoretically, the monograph's actual range is no greater than three. This level of substitution is not possible in practice, though.

Na CMC is considered insoluble above a commercial DS of 1.50. It was evident from the level of substitution attained that both sources of Na CMC were suitable for use from a business perspective.

Understanding the degree of polymerization aids in comprehending the substance's polymeric nature and potential future uses. It was 830 for C1 and 654 for C2. There may be species-to-species differences, though. However, it is evident that both sources can be utilized as polymers because of their higher degree of polymerization (above 440), as stated in the USP monograph for powdered cellulose.

3.3. Pharmacopoeia research on cellulose

While cellulose is soluble in strong acids and bases, it is insoluble in a variety of solvents, including water, ethanol, acetone, dil, mineral acid, and alcohol. The assay revealed that the α-cellulose content of C1 was 97.90%, whereas that of C2 was 99.17%. Both celluloses pass the suspension test, which indicates that the solid settles completely in 30 minutes after being ground with water. Drying loss was found to be 6.02% and 6%. C1 and C2 had pH values of 6.5 and 6.7, respectively. According to the water-soluble substance test, which should not exceed 1.5%, C1 had 1.23% residue and C2 had 1.1%. As a result, these samples contained no starch. The final test involved putting cellulose through an acid digestion process to determine the sample's lead content. Atomic absorption spectroscopy was used to verify it. Lead content was determined to be 0.467 mg/kg for C1 and 0.476 mg/kg for C2. Every test passed the USP monograph's limits for powdered cellulose.

3.4 Pharmacopoeial analysis of Na CMC

According to the solubility of both CMCs, they were insoluble in ether, acetone, and alcohol and produced a viscous colloidal solution when dissolved in water. Both CMCs pass the foam test, meaning that no foam layer forms when 0.1% of the solution is shaken. Since there is no precipitate when copper sulfate is added to the sample solution, the precipitate test is also successful for both CMCs. Color reaction tests are successful because the sulfuric acid reaction with CMC and 1-naphthol TS results in the development of a reddish-purple color at the interface. CMC1's LOD was 11.4%, while CMC2's was 10.2%. CMC1 and CMC2 had pH values of 7.6 and 7.7, respectively. For CMC1 and for, the sodium content was 6.85%. The assay results for CMC1 and CMC2 were 99.21% and 99.35%, respectively. For CMC2, water retention or swelling was favorable. CMC 1 and CMC 2 had lead contents of 0.478 and 0.441 mg/kg, respectively.

3.5. Water absorption and swellability level

CMC1 had superior swelling properties, as evidenced by its 98% swellability compared to 84% for CMC2. Water uptake is high at first, then gradually decreases, and after 20 minutes, it is very low. Since values are obtained above 100%, percentage values are calculated for 100% as standard.

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3.6. Cellulose and Na CMC Characterization

3.6.1. FT-IR The FT-IR graphs of C1 and C2 (Fig. 1) demonstrated the presence of –OH stretching close to 3300 cm-1. While the absorption is attributed to α-glycosidic bonding, which was the identification that the cellulose obtained is of pure form, the characteristic group for cellulose identification were near 2900, 1400, 1600, 1300, 1200, 1000 cm-1, and near 890 cm-1.

–CH2 symmetric bending was responsible for the absorption at 1400 cm-1, whereas –CH bending was responsible for the peak at 1350 cm-1. The –CH2 bending was attributed to the peak around 1320 cm-1. The C-OH skeletal vibration was identified as the peak at about 1100 cm-1, while the C-O-C pyranose ring was identified at about 1050 cm-1 (Zhang et al., 2015).

The characteristic groups were located close to 3600 cm-1, 2900 cm-1 (Biswal & Singh, 2004), 1600 cm-1, and 1400 cm-1 for the -OH group, alkyl -CH bending, aromatic -C=C, and carboxylic -OH bending, respectively, in the FT-IR graphs of CMC1 and CMC2 (Fig. 2). The graph demonstrated that group shifting eventually happened after the cellulose reacted correctly. The carboxymethyl group has been substituted, as evidenced by the peak that appeared around 1400 cm-1.

Previous studies' FT-IR data (Candido & Gonçalves, 2016) indicated that leaves' CMC was monosubstituted because the peak for -OH groups was seen above 3400 cm-1, indicating that only one -OH group was substituted and that DS was not above 0.4. However, this study's IR peak was seen close to 3400 cm-1, indicating that multiple free -OH groups are substituted and that the degree of substitution was also seen above 0.4.

3.6.2. The broad endothermic peaks in C1 and C2 were visible in the DSC DSC graph (Fig. 2). Both cellulose graphs show that cellulose has a melting point above 300°C. In both celluloses, degradation begins around 270°C. Additionally, both CMC1 and CMC2 exhibit broad endothermic peaks, with degradation beginning in both CMCs at about 210°C. These graphs' wide endothermic peaks attest to the samples' polymeric makeup.

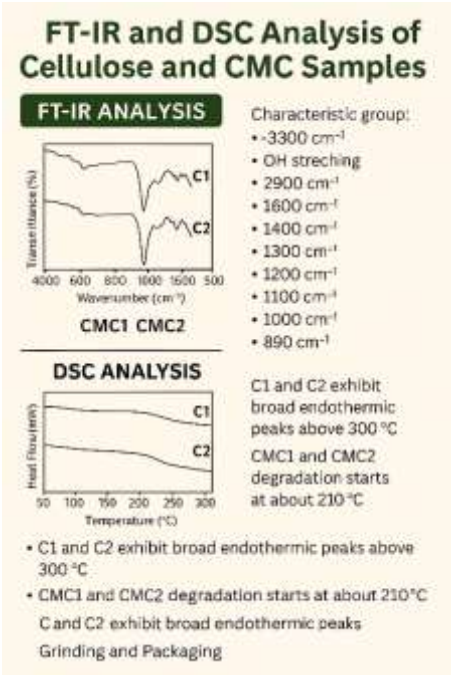

Figure 3FT-IR and DSC analyses confirm successful cellulose modification and thermal stability of synthesized Na-CMC.

3.6.3. Diffractogram of X-rays

The amorphous nature of the substances was revealed by X-ray diffraction (Fig. 3) of C1, C2, CMC1, and CMC2. The substance's powdery nature is confirmed by its amorphous nature. The presence of cellulose-I structure is indicated by the peaks between 2=19° and 22°.

3.6.4. SEM SEM images (Fig. 4) of C1 and C2 demonstrate thread-like structures with an uneven surface feature similar to those previously reported elsewhere (http://www.jrspharma.com/Arbocel-Powdered cellulose), indicating the success of extraction. These images also closely resemble SEM images of patented powdered cellulose. However, both CMC1 and CMC2's SEM images display smooth structures, indicating that substitution was successful. Images of CMCs showed intact fibers.

3.6.5. Zeta potential and particle size

The size of the particles for C1 and C2 ranged from 300 to 600 nm and 250 to 500 nm, respectively. This demonstrated that the particle size was in the nanometer range, and the XRD and SEM data confirm that cellulose is achieved at a very fine size. CMC1's particle size was between 400 and 600 nm, whereas CMC2's was between 1200 and 1900 nm. The PI index was deemed acceptable because it fell between 0.4-0.96, which was less than 1 for each of the four samples.

C1's zeta potential was 24.6 mV, while C2's was -2.5 mV. It was 46.6 mV for the CMC1 and 1.4 mV for the CMC2. C1 and CMC1 showed the highest positive zeta potential, indicating that they were the sample's stable form at positive pH. The opposite is true for C2 and CMC2, which may be because charge transfer is not possible at this pH. For these samples, a little more pH adjustment will be beneficial. However, it is possible to bring the pH into the positive range, which indicates that C1 and CMC1 will be the best polymers for use in pharmaceutical applications.

3.7. Results of formulation

In order to investigate the drug's release profile or the impact of Na CMC on the release profile of paracetamol, the solid dosage form of the model drug was formulated using synthesized Na CMC. Here, Na CMC served as a disintegrating agent. The 30-minute release profile makes it abundantly evident that the formulation containing CMC1 had a better profile than CMC2. This dissolution was carried out in a pH 6.8 phosphate buffer. After 30 minutes of dissolution, the release for CMC1 was 10.068 percent, and for CMC2, it was 8.55% (Chawla et al., 2014).

3.8. Pharmacoeconomics

Every step was costed, as stated in the experiment (Table 2-5). In other words, it was discovered that the cost of producing 100 kg of cellulose using these sources was lower than what was sold. However, the initial costing was based on the laboratory experiment and the raw material costs as they were purchased. Negotiation prices were then obtained for 100 kg by comparing the costs of different distributors (Table 6).

Put more succinctly, cellulose derived from sugarcane leaves is significantly less expensive than bagasse; consequently, the price of the semi-synthetic product eventually impacts it as well. Here, wood pulp and cotton linter are also taken into consideration for comparison. Since the market's starting materials are more expensive, subsequent products will also be more expensive. According to market research, the semi-synthetic industry's prices for larger amounts of cellulose used in food can range from Rs. 60 to Rs. 250. Therefore, cellulose made from these sources—which are wastes—is far less expensive.

The degree of polymerization also indicates that it can be used to synthesize semi-synthetic derivatives, and pharmaceutical data with pharmacopeial and pharmaceutical data clearly states that these sources, specifically sugarcane leaves, can be used efficiently to synthesize various derivatives. This means that using this source to synthesize semi-synthetic derivatives of efficient quality can be produced, and at cheaper prices.

In addition, using products that are synthesized from these sources will lower the cost of formulations that contain them because the cost of excipients will be low, which will lower the cost of formulations. Cost-minimization analysis is a component of this pharmacoeconomic research methodology.

The cost of formulations or the locations where this cellulosic product is used is ultimately impacted by the pharmacoeconomic analysis of the excipient based on its source. The cost differences between the synthesized and commercially available versions are clearly displayed in the study. Pharmacoeconomic studies are typically based on clinical factors and drug or drug-excipient relationships; however, in this case, the study was conducted for the synthesized excipients to support their use in a variety of fields that use cellulosic products.

4. Findings

In addition to successfully extracting cellulose from waste materials gathered from nearby farms, high-purity Na CMC was also produced from these celluloses and compared to pharmacopoeial standards. CMC1 achieved a good degree of swelling and water retention. In contrast to C1 and CMC1, the properties of C2 and CMC2 were favorable. C1 and CMC1 were stable, though. The degree of polymerization demonstrated cellulose's promising potential for the production of semi-synthetic derivatives. It is a cheap polymer that has both commercial and pharmaceutical applications, according to physicochemical analysis and pharmacoeconomics. Na CMC produced from the cellulose of sugarcane bagasse and leaves can be effectively utilized in pharmaceutical products, according to the pharmaceutical evaluation.

The degree of substitution was above 0.4 for both CMCs, indicating efficient substitution and the successful commercial aspect. Thus, the massive amounts of waste produced by sugarcane plantations can be used for commercial purposes. Such low-cost cellulose sources have a bright future, and their derivatives can be further explored in the pharmaceutical industry.

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