International Journal of Biological Macromolecules 281 (2024) 135865

Contents lists available at ScienceDirect

International Journal of Biological Macromolecules

journal homepage: www.elsevier.com/locate/ijbiomac

Review

Nanocellulose and microcrystalline cellulose from citrus processing waste: A review

Rosaria Ciriminna [a], Giovanna Li Petri [a], Giuseppe Angellotti [a], Enrica Fontananova [b], Rafael Luque [c,*], Mario Pagliaro [a,*]

[a] Istituto per lo Studio dei Materiali Nanostrutturati, CNR, via U. La Malfa 153, 90146 Palermo, Italy
[b] Istituto per la Tecnologia delle Membrane, CNR, via P. Bucci, cubo 17/c, 87036 Rende, CS, Italy
[c] Universidad ECOTEC, Km 13.5 Samborondón, Samborondón EC092302, Ecuador

ARTICLE INFO

Keywords:
Nanocellulose
Microcrystalline cellulose
Citrus cellulose
Citrus nanocellulose
Bioeconomy

ABSTRACT

Used since decades to produce pectin, citrus processing waste poor in lignin and rich in hemicellulose obtained from lemon and orange juice industrial manufacturing is ideally suited also as microcrystalline cellulose and nanocellulose raw material. The study merges the outcomes of chemistry and bioeconomy research between 2007 and early 2024 with technology and economic insight, to reach five conclusions that will hopefully inform practice-oriented work of researchers and bioeconomy company's managers interested in the sustainable manufacturing of these important biomaterials.

1. Introduction

Citrus processing waste (CPW) obtained from orange and lemon juice industrial production is used since decades as main raw material of pectin industrial production [1]. Fresh (wet) or dried peels are usually supplied to pectin manufacturers by citrus juice and essential oil (EO) manufacturers. Production takes place via hydrolytic extraction with mineral acid followed by precipitation with alcohol and recovery of alcohol under vacuum [2]. Pectin is the most valued food hydrocolloid, and since the early 2010s its demand is growing at fast annual growth rate driven by large demand in the food and beverage industries as texturizer, gelling agent and thickener [3], as well as by numerous new practical applications of pectin in medical, personal care, cosmetic and nutraceutical functional products [4] Upon drying, the cellulose-rich insoluble residue of pectin production is either burned to produce heat, or supplied to biodigestors wherein bacteria convert it into biogas (a mixture of carbon dioxide and methane) [5]. The use of CPW, poor in lignin and rich in hemicellulose (see below), has long been investigated for what Seisl and Hengstmann have called a more sustainable production of "manmade cellulosic fibers" [6]. More in general, awareness of the huge loss of valued substances including flavonoids, sugars and organic acids abundant in CPW has translated into intense research work aimed at establishing the "biorefinery of orange peel" [7].

In practice, most orange juice producers also produce lemon, grapefruit and tangerine juice. Hence, in principle, the new chemical, physical and biochemical (enzymatic) routes to valued bioproducts beyond pectin (including citrus cellulose, flavonoids, sugars and terpenes) can be applied to all citrus fruits. From a practical standpoint, *Citrus* is the second most cultivated fruit globally, with nearly 162 million tonnes of fruits harvested in 2021, of which oranges reached ~76 million t [8].

The global orange (*Citrus sinensis*) juice production in the 2019/2020 season was 1.7 million t [9]. For comparison, the global production volume in 2014/2015 was 1.83 million t. These values, however, refer to the main product of the industry which is frozen concentrated orange juice (FCOJ), namely the frozen juice obtained after evaporating under vacuum 90 % of the water contained in the fresh juice. The weight amount of orange processing waste (OPW) is about 50 % of the fruit undergoing industrial squeezing. Only in Brazil, half of the 20–22 million tonnes harvested yearly are used to produce the aforementioned FCOJ, generating 10–11 million t of OPW.

Summarizing achievements between 2007 and early 2024, this study suggests that this agro-industrial waste may shortly become a key raw material of the nanocellulose and microcrystalline cellulose (MCC) industries. Industrially manufactured since the early 1960s from wood pulp cellulose hydrolyzed with an excess of mineral acid at temperature above 100 °C, MCC consists of highly crystalline cellulose whose degree of polymerization has been reduced by the acid hydrolysis to about 400

---

* Corresponding authors.
E-mail addresses: rluque@ecotec.edu.ec (R. Luque), mario.pagliaro@cnr.it (M. Pagliaro).

https://doi.org/10.1016/j.ijbiomac.2024.135865
Received 6 May 2024; Received in revised form 6 September 2024; Accepted 19 September 2024

[10]. Widely used in the pharmaceutical industry for tableting, MCC is increasingly used in the food (texturizer, anti-caking agent, fat substitute, emulsifier, extender, and a bulking agent), and personal care and cosmetic industries. The global market exceeded $1 billion in economic value in 2022 [11].

Though commercially available in the form of cellulose nanofiber (CNF), cellulose nanocrystal (CNC), or bacterial cellulose (BC), nanocellulose is an expensive functional bioproduct whose numerous potential applications so far have been limited by its high price. In general, harsh chemical conditions and large amounts of energy and harmful chemical compounds are used in the production of CNF and CNC [12], whereas BC industrial synthesis from glucose using *Gluconoacetobacter xylinus* bacteria is expensive and the production and isolation methods inefficient [13].

The following analysis merges the outcomes of chemistry and bioeconomy research between 2007 and early 2024 with industrial and economic insight, to reach five main conclusions that will hopefully inform practice-oriented work of researchers and bioeconomy company's managers interested in the sustainable manufacturing of these important biomaterials.

2. Results and discussion

2.1. Citrus nanocellulose

In 2014, Endo and co-workers in Japan were the first to report a two-step method to obtain nanocellulose from mandarin (*C. unshiu*) industrial processing previously purified via the removal of essential oil and pigments with hot aqueous EtOH [14]. The team treated the purified CPW at a solid concentration of 1.0 wt% with 0.18 wt% HCl at 120 °C for 2 h at 1.2 bar in an autoclave. A highly diluted water suspension (0.0001 wt%) of the hydrolyzed CPW underwent sonication for 15 s eventually affording nanocellulose fibrils (Fig. 1c). The fibrils has relatively low crystallinity index (CI) of 58 %. Remarkably, the nanofiber width of 2–3 nm corresponds to the width (2.5 nm) of the single crystal.

The dispersion showed high colloidal stability ascribed to the low amount of galacturonic acid moieties of the residual pectin fibers whose negative charge facilitates the dispersion of the nanofibrils and prevents their subsequent aggregation. Considering the good yield (8.9 wt%) of cellulose nanofibrils from mandarin peel waste, Endo and co-workers concluded that these cellulose nanofibrils "can be utilized as highly valued nanomaterials" [14].

A few months later, Zain and co-workers in Malaysia reported the production of nanocellulose from pomelo (*C. grandis*) albedo [15]. CNC was obtained using concentrated (65 wt%) sulfuric acid at 45 °C for 45 min of dried albedo powder previously freed from lignin and hemicellulose via alkali (4 wt% NaOH) treatment at high temperature followed by bleaching with $NaClO_2$ (1.7 wt%) at 110–130 °C for 4 h. The resulting nanocellulose is comprised of 100–150 nm rod-shaped nanoparticles having CI 60 % (analogous to that of mandarin nanocellulose [14]), and excellent water holding capacity (12.75 $g_{water}/g_{cell.}$).

In 2015 Labic and co-workers in Brazil were first to report the enzyme-mediated hydrolytic production of CNF from *Citrus sinensis* processing waste [16]. CPW was again deglinified with alkali, after which it underwent hydrolysis using a bacterial enzyme cocktail derived from *Xanthomonas axonopodis* pv. *citri* for 48 h at 45 °C followed by bleaching with $NaClO_2$ (1.7 % w/v). Eventually, a dilute (1 % w/v) suspension of the hydrolyzate following dialysis underwent sonication for 12 min affording rod-shaped cellulose nanofibers with 55 % CI. The nanofibrils were 10 nm large and with an average length of ~460 nm, substantially longer than nanocellulose fibers obtained via enzymatic treatment of cotton and sugarcane cellulose fibers.

Recognizing that enzymatic hydrolysis "involves high production cost" because "it requires the use of purification techniques for enzymes' concentration" [17], the same team three years later reported a multistep route to citrus nanocellulose involving numerous chemical steps followed by ultrasound treatment of the cellulose obtained. In detail, industrial CPW underwent sequential hydrothermal treatment with aqueous HCl (5 % v v^{-1}) at 100 °C, followed by aqueous NaOH (3.0 % m v^{-1}) at 120 °C, and bleaching with $NaClO_2$ at 80 °C. After an additional bleaching step using aqueous H_2O_2 at pH 10 and 80 °C for 30 min, eventually an ultrasound treatment yielded CNF consisting of 20 nm wide nanofibers with 72 % crystallinity [17].

The first chemical-free route to citrus nanocellulose was reported in 2016 by scholars in Thailand at a conference (and subsequently published in a journal's issue including selected conference proceedings) [18]. The team autoclaved at 120 °C the lime (*Citrus* × *aurantiifolia*) juice extraction residue to successfully remove most hemicellulose and pectin from the native fiber, followed by high shear homogenizing (at 20,000 rpm) for 15 min, and high pressure homogenizing at 400 bar for 5 passes. The lime nanocellulose fibers obtained (Fig. 2) had diameter in the 3–10 nm range and CI of 65 %.

In brief, the hydrothermal treatment by autoclaving at the temperatures higher than 110 °C promotes the autohydrolysis of hemicellulose (and the hydrolysis of pectin) through the acetic acid molecules liberated from the acetyl groups of xylan (backbone of hemicellulose).

The subsequent year Matharu and co-workers in Great Britain reported the hydrothermal treatment using microwaves of orange CPW previously "depectinated" via acid-free microwave-assisted heating (at 120 °C for 15 min) [19]. Heating at temperature between 120 and 200 °C afforded mesoporous materials comprised of nanocellulose fibrils, cellulose crystals, and residual amorphous matter. Furthermore, lignin residues and inorganic salt (calcium oxalate) were also present. As a result, the materials were deeply colored in grey/brown. Not suitable for application as nanomaterials, these materials had good hydration capacities (12–23 $g_{water}/g_{cell.}$) making them suitable as water adsorbents.

Another chemical-free route to micronized cellulose was reported

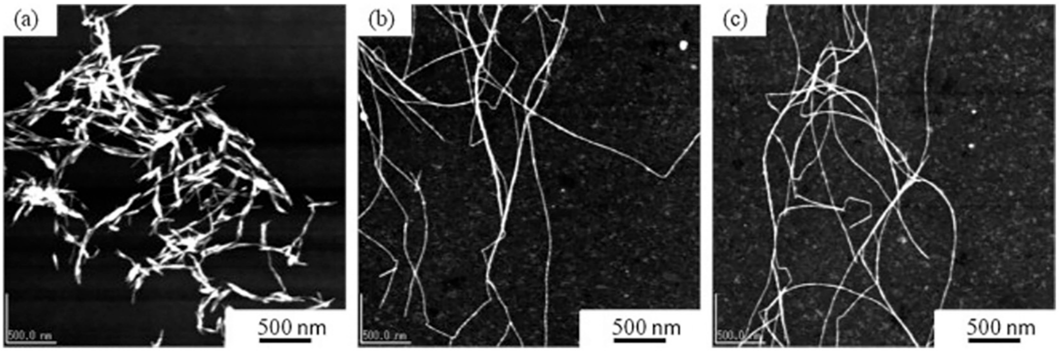

Fig. 1. AFM (a) disk-milled wood cellulose, (b) sonicated multistep, and (c) hydrothermally treated mandarin peel waste. [Reproduced from Ref. [14], with kind permission].

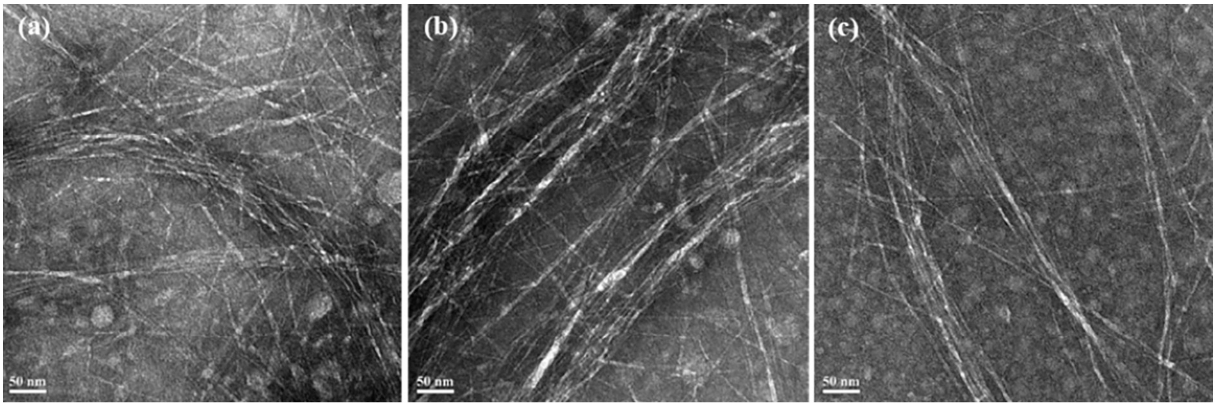

Fig. 2. TEM of nanofibrillated cellulose prepared using different autoclaving conditions; (a) 110 °C, (b) 120 °C and (c) 130 °C. [Reproduced from Ref. [18], with kind permission].

from Italy in 2021 when Pagliaro's and Meneguzzo's teams reported the discovery of "CytroCell" obtained via hydrodynamic cavitation (HC) of industrial lemon (and grapefruit) processing waste carried out in water only [20]. A new micronized cellulose of low crystallinity, high porosity, good water holding capacity and good dispersibility was obtained directly on a semi-industrial scale processing in a HC reactor >40 kg of wet lemon or grapefruit processing waste in 120 L water. The method extracts in one pot all the main bioproducts of CPW, with the soluble fraction consisting of a new, highly bioactive citrus pectin dubbed "IntegroPectin" [21].

In the case of lemon agro-industrial waste, CytroCell consists of 0.5–3 μm long cellulose microfibrils whose section varies between about 110 and 420 nm (Fig. 3), whereas grapefruit CytroCell consists of ramified cellulose microfibrils whose diameter varies from 500 nm to 1 μm [22]. In other words, HC converts native cellulose in citrus processing waste into micronized fibers ready for use in advanced nanomaterial applications without the need of chemicals or of auxiliary fibril individualization treatment such as sonication or high pressure homogenizing.

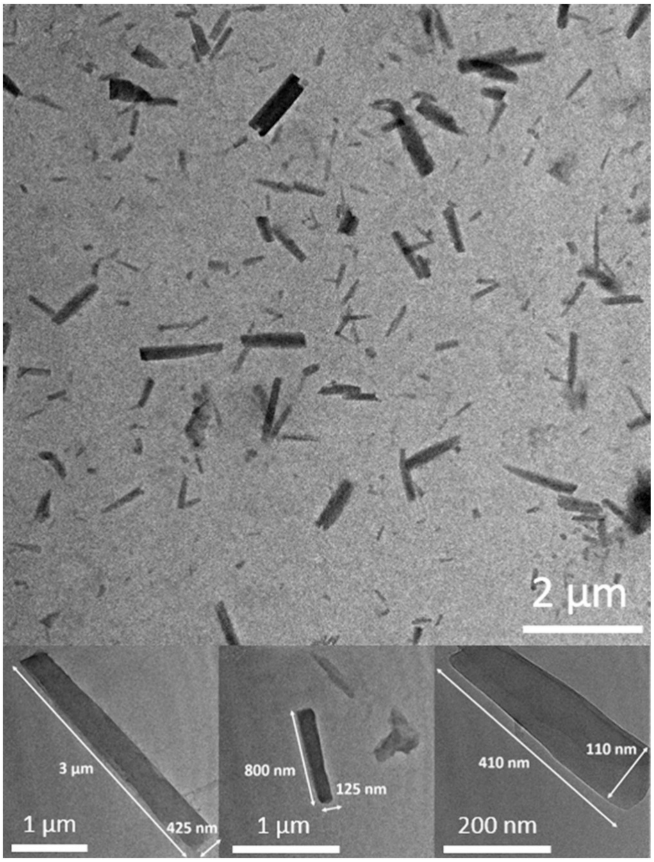

Fig. 3. TEM images of lemon CytroCell (*top*) and after focusing on selected single fibrils (*bottom*). [Reproduced from Ref. [22], with kind permission].

As put it be Endo commenting in 2017 the low industrial uptake of nanocellulose the price "remained high because people prefer thinness, such as a few nm to 10 nm. If we can demonstrate that sufficient performance can be achieved even with fibers of micron or submicron sizes, the price will go down and the materials are likely to become more popular" [23]. Rather than achieving "sufficient performance with fibers of micron or submicron sizes", micronized cellulose can be dissolved in a suitable solvent freeing the aggregated microfibrils into nanofibrils. Lemon CytroCell, for example, can be dissolved in biobased dihydrolevoglucosenone (tradenamed Cyrene), an aprotic "green" solvent of low acute oral toxicity [24] that brings in solution the nanofibrils comprising the submicron fibers.

Dispersed in water, the lemon CytroCell nanofibrils could be successfully used to stabilize the otherwise chemically unstable and mechanically weak membranes made of polymerizable ionic liquid (PIL) comprised of a sytrene unit functionalized with a triethylphosphonium ion and BF_4^- as counter ion [25]. A strong transparent anion exchange membrane (AEM) highly stable in concentrated alkali solution was obtained (Fig. 4), which is highly promising towards the development of new generation AEMs for highly efficient water alkaline electrolysis.

Besides largely improving the aspect ratio (length/diameter) of the citrus nanocellulose nanofibrils eventually coordinating with the polymer matrix, the mechanical properties of the membrane are further optimized by the better alignment of the nanofibrils upon casting. In general, indeed, more aligned fibrils have higher tensile strength (300–500 MPa, [26]), while aspect ratios larger than 50 ensure a highly efficient reinforcing effect [27].

We briefly remind that the reinforcing effect of nanocellulose in composites with polymer is due to long nanofibers reaching the percolation threshold at low loading levels (between 1 and 6 vol% depending on the cellulose source) [28], when the rigid cellulose nanofibrils form a network within the nanocomposite due to percolation of the nanofibrils [29].

The discovery of CytroCell allows to overcome the main drawback related to the use of nanocellulose in polymer composites, namely the inherent difficulty to disperse the highly polar cellulose nanofibrils in non-polar media, that so far limited the effective incorporation of cellulose nanocrystals as polymer reinforcing agents only to polar media [28]. We remind that in the empirical $E_T(30)$ solvent polarity scale, polarities of celluloses cover a wide section of 49–57 kcal mol^{-1}

Fig. 4. Lemon CytroCell@PIL anion exchange membrane (photo courtesy of M. Pagliaro).

corresponding to 1-pentanol [$E_T(30) = 49.1$ kcal mol^{-1}] and formamide [$E_T(30) = 56.6$ kcal mol^{-1}] as solvents [30a]. This fact, summarized by the ancient statement *corpora non agunt nisi soluta* (substances do not react unless dissolved) is generally valid also in cellulose chemistry [30b], and is of high relevance also in the case of nanocellulose practical applications.

The high solubility of CytroCell in Cyrene can be explained by the: *i*) poor packing of cellulose chains in crystals which tends to make it more soluble, *ii*) charges introduced along the polymer chain due the introduction of organic functionalities in the cellulose backbone that decreases the hydrogen-bond donating ability (α) [30a], and *iii*) amphiphilic nature of Cyrene solvent, having both polar and nonpolar parts. Cellulose, indeed, is an amphiphilic polymer with hydrophobic interactions explaining the solubility pattern of cellulose in selected solvents [31].

Contrary to citrus nanocellulose obtained from Kinnow mandarin (*C. reticulata*) when the multistep alkaline-acid treatment affords CNC of increased crystallinity (compared to native cellulose) [32], cavitation of lemon processing waste disrupts the cellulose crystallinity affording disordered cellulose microparticles in which negative charges are present in the repeat cellobiose units due to partial esterification reaction of primary alcohol groups in native cellulose with residual citric acid [20].

Table 1 summarizes selected studies reviewed in this paragraph devoted to citrus nanocellulose and method of isolation.

2.2. *Citrus microcrystalline cellulose*

Amid agro-industrial wastes, citrus peel is a particularly attractive non-wood raw material also for MCC. In 2007, Ejikeme in Nigeria was first to report that a simple alkali-bleaching treatment of orange peel followed by hydrolysis with mineral acid affords MCC of excellent quality [33]. In detail, orange peel previously dried and powdered underwent the alkaline bleaching hydrothermal treatment to remove lignin using NaOH 4 wt% for 180 min at 80 °C followed by bleaching (5.3 wt% $NaClO_2$ and 9.3 wt% H_2O_2). The crude cellulose obtained was hydrolyzed with 2.5 M HCl at 105 °C for 15 min. Chiefly consisting of 53 μm flower-like microparticles, orange MCC had 2.92 $g_{water}/g_{cell.}$ water holding capacity, and ultralow ash (0.035 %) and 4.9 % moisture content.

Six years later, in 2013, scholars in Romania reported an improved method to extract MCC from orange peel, based on prolonged heating at 105 °C for 317 min the powdered peel kept in a rotovapor added with aqueous NaOH (38.2 wt%) combined with chelating agent EDTA (9.56 wt%) [34]. The latter ethylenediaminetetraacetic acid is able to remove the otherwise insoluble protopectin, pectic acid and its calcium and magnesium salts, affording high yield (~26 %) of MCC mostly consisting of alpha cellulose (85.8 %). The resulting MCC had CI of 68.7 % and relatively low degree of polymerization (312).

These results were rediscovered in the late 2010s with the emergence of the bioeconomy. In 2018, scholars in China and the USA reported that MCC of excellent quality can be readily extracted also from pomelo

Table 1
Selected studies on citrus nanocellulose.

Study title (Ref.)	Year	Isolation method
Isolation of cellulose nanofibrils from mandarin (*Citrus unshiu*) peel waste (14)	2014	Acid hydrolysis at 120 °C for 2 h at 1.2 bar
Preparation and characterization of cellulose and nanocellulose from pomelo (*Citrus grandis*) albedo (15)	2014	Acid hydrolysis at 45 °C following alkaline hydrolysis and bleaching
Enhanced materials from nature: nanocellulose from citrus waste (16)	2015	Enzymatic hydrolysis
A multistep mild process for preparation of nanocellulose from orange bagasse (17)	2018	Acid hydrolysis at 100 °C, followed by alkaline hydrolysis, bleaching, and ultrasound treatment
Production of nanocellulose from lime residues using chemical-free technology (18)	2018	Autoclaved at 120°, followed by high shear homogenizing (at 20,000 rpm), and high pressure homogenizing at 400 bar for 5 passes.
The Hy-MASS concept: *hydrothermal microwave assisted selective scissoring of cellulose for* in situ *production of* (meso)porous *nanocellulose fibrils and crystals* (19)	2019	Hydrothermal treatment with microwaves following acid-free microwave-assisted heating at 120 °C
CytroCell: valued *cellulose from citrus processing waste* (20)	2021	Hydrodynamic cavitation in water only
Management of citrus waste by switching in the production of nanocellulose (32)	2016	Multistep alkaline-acid hydrolysis

(*Citrus grandis*) peel via the aforementioned two-step process (alkaline bleaching treatment followed by acid hydrolysis) [35]. In detail, pomelo peel powder was treated with a 4 % (w/w) NaOH solution containing 0.9 % (v/v) H_2O_2 at 80 °C for 4 h. Hence, the crude cellulose was treated 15 min with a mixture of 80 % acetic acid-68 % nitric acid (v/v = 10:1) at 100 °C to remove residual hemicellulose and lignin and hydrolyze cellulose. The resulting MCC consisted of non-aggregated microparticles shorter and less regular (less smooth) when compared to the rod-shaped, relatively smooth microparticles comprising commercial MCC (Fig. 5).

Coupled to substantially lower CI compared to that of commercial MCC (40.5 % vs. 72.1 %), this explains also the significantly better water (10.14 vs. 2.64 $g_{water}/g_{cell.}$) and oil (5.29 g/g vs. 2.73 $g_{oil}/g_{cell.}$) holding capacity than commercial MCC. Noting that pomelo MCC still had good thermal stability, starting to decompose at 280 °C vs. 291 °C of commercial MCC, the team concluded that it would be "an excellent emulsion stabilizer, dietary fiber supplement, and fat substitute" [35].

The method is general and can be applied to any citrus fruit peel. Indeed three years later scholars in China used it to extract MCC from lemon peel with a slight modification (replacing the HOAC/HNO_3 solution with a 6 wt% HCl solution). The team obtained excellent 15.3 % yield of lemon MCC [36]. Isolated via freeze drying, the latter MCC was dissolved in 1-butyl-3-methylimidazolium chloride (BmimCl), followed by direct regeneration in water to form hydrogels, thereby establishing a facile and green dissolution-regeneration method, using BmimCl as a solvent and water as a regenerated solvent. It was enough to add 0.6 g of lemon peel powdered to 0.6 g of lemon MCC previously dissolved in 30 g BmimCl to obtain a hydrogel of excellent adsorption capacity towards methylene blue (57.54 mg/g). The team ascribed the outcome to the non-cellulosic hemicellulose and lignin components of lemon peel that, upon solidification in the hydrogel, afford a hydrogel with a more uniform, sheet-like skeletons with porous morphology of largely enhanced adsorption capacity [36].

Since then, methods to extract MCC from citrus fruit peel have continued to rely on alkali treatment followed by acid hydrolysis, replacing bleaching with chlorine-containing compounds with non-toxic 40 % hydrogen peroxide [37] or with ultrasound-assisted alkaline hydrolysis at 80 °C using diluted hydrogen peroxide [38].

Table 2 summarizes selected studies reviewed in this paragraph devoted to citrus microcrystalline cellulose and method of isolation.

2.3. Economic and industrial aspects

Following pectin, soluble sugars, and hemicellulose, cellulose is the most abundant bioproduct in orange peel. The amount if lignin is lower than 0.85 % (Table 3) [39].

In 2022, the world's largest orange juice manufacturer announced

Table 2
Selected studies devoted to citrus microcrystalline cellulose and method of isolation.

Study title (Ref.)	Year	Isolation method
Investigation of the physicochemical properties of microcrystalline cellulose from agricultural wastes I: orange *mesocarp* (33)	2007	Alkali-bleaching treatment followed by acid hydrolysis
Optimization of isolation of cellulose from orange peel using sodium hydroxide and chelating agents (34)	2013	Alkaline hydrolysis at 105 °C combined with EDTA
Isolation and characterization of microcrystalline cellulose from pomelo peel (35)	2018	Bleaching alkali treatment followed by acid hydrolysis
Direct regeneration of hydrogels based on lemon peel and its isolated microcrystalline cellulose: Characterization and application for methylene blue adsorption (36)	2021	Bleaching alkali treatment followed by acid hydrolysis
Synthesis and suitability characterization of microcrystalline cellulose from *Citrus x sinensis* sweet orange peel fruit waste-based biomass for polymer composite applications (37)	2024	Alkali treatment followed by acid hydrolysis and bleaching with 50 % hydrogen peroxide
Physicochemical properties and structure characterization of microcrystalline cellulose from pomelo fruitlets (38)	2022	Ultrasound-assisted alkaline hydrolysis and bleaching with hydrogen peroxide at 80 °C

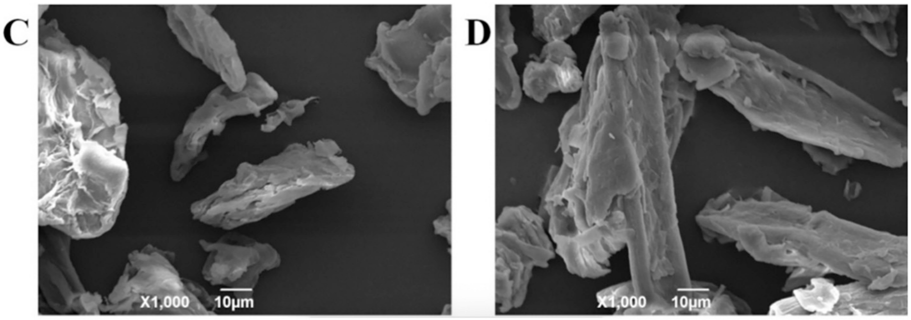

Fig. 5. SEM images of pomelo MCC (C) and commercial MCC (D). [Reproduced from Ref. [35], with kind permission].

Table 3
Chemical composition of orange peel (in percentage) [Reproduced from Ref. [39], with kind permission].

Pectin	Soluble sugar	Hemicellulose	Cellulose	Protein	Ash	Fat	Lignin	Others
42.5	16.90	10.50	9.21	6.50	3.50	1.95	0.84	4.35

the launch of another company's unit (named Evera) that "as a result of years of research and the use of intensive technology", developed a number of "natural ingredients for different industries through the means of reuse technology of waste of the orange such as husks, peels, leaves, flowers, and seeds" that can be "utilized in the food and beverage market, improving the healthiness and the nutritional value of the end products" [40]. Amid said new ingredients, the company started commercialization of a new hydrocolloid comprised of dehydrated orange fiber of very low caloric index (10.2 kcal/100 g) and high fiber content (3.34 g/100 g). The soluble pectin fibers are intertwined with the insoluble cellulose and hemicellulose fibrils affording a hydrocolloid well suited as thickener, stabilizer and gelling agent in a variety of beverage, dairy, food and nutraceutical products [41]. Similar products are commercialized by companies based in New Jersey [42] or in Sicily [43].

The production of these citrus (orange and lemon) fibers requires only CPW delignification with alkali, allowing citrus manufacturing companies to avoid the substantial capital and operating costs of a pectin production plant. Even in the case of complete EO and pigment removal to produce flavor-free orange fiber, this is achieved using a green and easily recoverable solvent such as EtOH. In this way, the citrus processing industry's main by-product, previously dealt with as an agro-industrial waste of negative value, is converted into a valued ingredient for the food and nutraceutical industries.

Getting to MCC, the price is generally high. In 2010, the price was in the range €4–10/kg, dependent on product particle size distribution and purity [44]. By June 2023, however, highly pure MCC for pharmaceutical use manufactured abroad was sold in India at ~20 $/kg [45]. Furthermore, purity requirements (ultralow nitrite level) for MCC of pharmaceutical grade suddenly increased in 2018 following the discovery of harmful *N*-nitrosoamines in several drug products using MCC as excipient [46]. Nitrosamines form due to reaction of secondary or tertiary amines present in active pharmaceutical ingredients, as reaction by-product or as impurities, with a nitrosating agent like nitrous anhydride formed from the protonation of nitrite present in wood cellulose during acid hydrolysis.

Reputed market analysts recently suggested that the key driver of MCC market expansion will be its lower price made possible by the replacement of wood cellulose with non-wood sources, leading to a cheaper price of MCC, that in its turn "will fuel the increasing consumption of microcrystalline cellulose across different segments" [10]. Similar arguments are valid also in the case of nanocellulose: the use of citrus peel is particularly convenient because the raw material is poor in lignin and widely available at little or no cost from citrus juice manufacturers.

The global production of all main *Citrus* fruits between 1961 and 2021 has grown at significant rate (Fig. 6) [8]. Orange, with 75.57 million t fruit, is by far is the most widely cultivated citrus fruit, followed by tangerines (41.95 million t), limes and lemons (20.83 million t). Besides, pomelos and grapefruits (*C. paradisi* and *C. máxima*) have a production of 9.56 million t and other citrus fruits (*C. medica*, *C. bergamia*, *C. myrtifolia* and *Fortunella* spp.) have a production of 13.90 million t.

Brazil is by far the largest orange juice producer, accounting for three-quarters of global orange juice production and exports. Globally, the industry had revenues approaching $5 billion in 2023, expected to grow at 6 % annual growth rate until 2028 [47]. Until 2020, the industry was challenged to replace the FCOJ with not from concentrate (NFC) juice, as consumers in the main 40 markets (including the USA, Canada, and Europe) looking for more natural products reduced consumption of FCOJ by 23 % in just sixteen years between 2003 and 2018 [48]. In 2020 the COVID-19 public health crisis led to a sudden surge in sales of orange juice. In the USA, for instance, sales of the juice during 2020 soared (+16 % in annual volume sales compared to 2019), with sales remaining strong in 2021, until the high consumer price inflation rate of 2022 led to substantial declines in volume sales in late 2022 [49].

In this highly dynamic economic context, as mentioned above citrus juice producers and food ingredient manufacturers started to internalize the production of citrus peel-based food hydrocolloids made of intertwined cellulose, hemicellulose and pectin fibers [41–43]. As suggested in the conclusions, production of citrus MCC and citrus nanocellulose might likely follow soon.

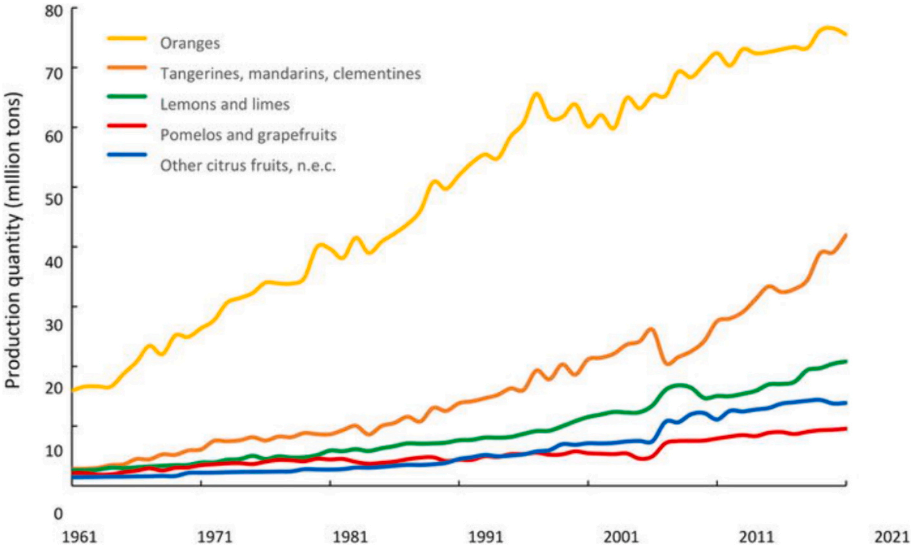

Fig. 6. World production of different citrus fruits between 1961 and 2021. [Reproduced from Ref. [8], Creative Commons Attribution 3.0 License].

3. Conclusions

In conclusion, the outcomes of the present study merging the results of recent chemistry and bioeconomy research with technology and economic insight, suggest that citrus agro-industrial waste obtained after citrus juice production may shortly become an important raw material for MCC and nanocellulose industrial production. The following five main conclusions may further inform work of researchers and bioeconomy company's managers interested in the sustainable manufacturing of these important biomaterials.

First, driven by global megatrends concerning health and the environment, the demand of biobased products and natural ingredients is growing at such high rate that it has become in a few years a significant production area of the chemical industry [50].

Second, a number of new technically and economically viable green chemistry routes to nanocellulose [51] and MCC [52] have been developed that are suitable for large scale industrial production at a fraction of the cost of current manufacturing technologies. These methods include autoclaving of CPW followed by high-pressure homogenization that effectively disintegrates the native cellulose fibers into nanoscale fibers [18] and cavitation (both acoustic and hydrodynamic) affording micron and submicron cellulose microparticles [53].

Third, the use of citrus processing waste as raw material improves the sustainability of nanocellulose and MCC production thanks to improved land utilization due to short growth cycle typical of agricultural residues as well as to its composition much lower in lignin and hemicellulose than wood. A lower lignin content improves the fibrillation efficiency of cellulose fibers, whereas hemicellulose enhances the properties of nanocellulose chiefly thanks to enhanced fiber swelling and fibrillation due to its hydrophilic and amorphous nature [54].

Fourth, the newly discovered solubilization of micronized citrus CytroCell cellulose in biobased Cyrene in principle allows to create all sort of cellulose-based materials (nanopaper, films, membranes, fibers, aerogels, hydrogels, composites etc.) in regenerated citrus cellulose nanofibrils, a feature so far restricted only to regenerated cellulose fibrils dissolved in costly ionic liquids [55].

Fifth, aware of the increasing economic value and production volumes of pectin [2,3], MCC [10] and nanocellulose [56], citrus juice producers are increasingly interested in turning into bioeconomy companies sourcing new and significant economic value (revenues) from their main production by-product (CPW).

We have recently shown that access to an economically viable green chemistry production route is not per se sufficient for an economically successful bioproduction, because access to cheap and abundant biobased raw material *and* a high bioproduct selling price are also required [57]. Citrus fruits are the second most produced fruit worldwide (162 million tonnes produced in 2021) [8], and the price for both MCC and nanocellulose (both CNC and CNF) is high. Hence, in conclusion, citrus processing waste is a technical and economically viable raw material that might replace expensive wood pulp in the forthcoming commercial production of cellulose nanofibrils and microfibrils based on new green chemistry routes to nanocellulose and microcrystalline cellulose [51,53].

CRediT authorship contribution statement

Rosaria Ciriminna: Writing – review & editing, Methodology, Conceptualization. **Giovanna Li Petri:** Visualization, Investigation, Data curation. **Giuseppe Angellotti:** Visualization, Investigation, Data curation. **Enrica Fontananova:** Writing – review & editing, Investigation, Data curation. **Rafael Luque:** Writing – review & editing, Methodology, Conceptualization. **Mario Pagliaro:** Writing – original draft, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No new data have been produced in this work.

Acknowledgments

This work is dedicated to Professor Takashi Endo, National Institute of Advanced Industrial Science and Technology, Japan, for all he has done to advance the science and technology of nanocellulose. This work was supported by the Ministero delle Imprese e del Made in Italy under the Piano Operativo della Ricerca "Ricerca e sviluppo sull'idrogeno" financed by the EU NextGenerationEU - M2C2 Investment 3.5, in the framework of the project PNRR Ricerca e Sviluppo sull'Idrogeno 2022-2025 - Accordo di Programma "Idrogeno" (PRR.AP015.017.002), "Obiettivo 1 - Produzione di idrogeno verde e pulito", "LA 1.1.6 – Sviluppo di materiali e componenti non contenenti materiali critici per elettrolizzatori anionici (AEM) operanti anche ad elevate pressione differenziale". Work of G.A. and G.L.P. was respectively supported by European Union NextGenerationEU - PNRR Sicilian Micro and Nano-Technology Research and Innovation Center Innovation Ecosystem (SAMOTHRACE, Mission 4, Component 2 - Investment 1.5 ECS00000022 - CUPB63C22000620005) and Made in Italy Circolare e Sostenibile (MICS, Mission 4, Component 2 - Investment 1.3, PE00000004, CUPB53C22004060006).

References

[1] R. Ciriminna, A. Fidalgo, R. Delisi, L.M. Ilharco, M. Pagliaro, Pectin production and global market, Agro Food Ind Hi Tech 27 (5) (2016) 17–20.
[2] Z.K. Muhidinov, K.I. Ikromi, A.S. Jonmurodov, A.S. Nasriddinov, S.R. Usmanova, J. T. Bobokalonov, G.D. Strahan, L.S. Liu, Structural characterization of pectin obtained by different purification methods, Int. J. Biol. Macromol. 183 (2021) 2227–2237, https://doi.org/10.1016/j.ijbiomac.2021.05.094.
[3] D. Seisun, N. Zalesny, Strides in food texture and hydrocolloids, Food Hydrocoll. 117 (2021) 106575, https://doi.org/10.1016/j.foodhyd.2020.106575.
[4] R. Ciriminna, A. Fidalgo, A. Scurria, L.M. Ilharco, M. Pagliaro, Pectin: new science and forthcoming applications of the most valued hydrocolloid, Food Hydrocoll. 127 (2022) 107483, https://doi.org/10.1016/j.foodhyd.2022.107483.
[5] C. Sabater, M. Villamiel, A. Montilla, Integral use of pectin-rich by-products in a biorefinery context: a holistic approach, Food Hydrocoll. 128 (2022) 107564, https://doi.org/10.1016/j.foodhyd.2022.107564.
[6] S. Seisl, R. Hengstmann, Manmade cellulosic fibers (MMCF) - a historical introduction and existing solutions to a more sustainable production, in: A. Matthes, K. Beyer, H. Cebulla, M.G. Arnold, A. Schumann (Eds.), Sustainable Textile and Fashion Value Chains, Springer, Cham, 2021, https://doi.org/10.1007/978-3-030-22018-1_1.
[7] J.Á. Siles López, Q. Li, I.P. Thompson, Biorefinery of waste orange peel, Crit. Rev. Biotechnol. 30 (2010) 63–69, https://doi.org/10.3109/07388550903425201.
[8] M. Pereira Gonzatto, J. Scherer Santos, Introductory chapter: world citrus production and research, in: M. Pereira Gonzatto, J. Scherer Santos (Eds.), Citrus Research - Horticultural and Human Health Aspects, IntechOpen, London, 2023, https://doi.org/10.5772/intechopen.110519.
[9] Statista, Orange juice production volume worldwide from 2014/2015 to 2022/2023 (in million metric tons), Hamburg. https://www.statista.com/statistics/1044906/world-orange-juice-production/, 2024 (accessed on April 8, 2024).
[10] D. Trache, M.H. Hussin, C.T. Hui Chuin, S. Sabar, M.R.N. Fazita, O.F.A. Taiwo, T. M. Hassan, M.K.M. Haafiz, Microcrystalline cellulose: isolation, characterization and bio-composites application - a review, Int. J. Biol. Macromol. 93 (2016) 789–804, https://doi.org/10.1016/j.ijbiomac.2016.09.056.
[11] Technavio, Microcrystalline Cellulose (MCC) Market by Application, Material and Geography - Forecast and Analysis 2023–2027, London, 2023.
[12] C. Yadav, A. Saini, W. Zhang, X. You, I. Chauhan, P. Mohanty, X. Li, Plant-based nanocellulose: a review of routine and recent preparation methods with current progress in its applications as rheology modifier and 3D bioprinting, Int. J. Biol. Macromol. 166 (2021) 1586–1616, https://doi.org/10.1016/j.ijbiomac.2020.11.038.
[13] B. Alriksson, cit. in: S. Matthis, Bacterial nanocellulose can become a strength enhancer, pulpapernews.com. www.pulpapernews.com/20190803/9456/bacterial-nanocellulose-can-become-strength-enhancer, May 2, 2018 (accessed August 5, 2024).

[14] S. Hiasa, S. Iwamoto, T. Endo, Y. Edashige, Isolation of cellulose nanofibrils from mandarin (*Citrus unshiu*) peel waste, Ind. Crop. Prod. 62 (2014) 280–285, https://doi.org/10.1016/j.indcrop.2014.08.007.

[15] N.F.M. Zain, S.M. Yusop, I. Ahmad, Preparation and characterization of cellulose and nanocellulose from pomelo (Citrus grandis) albedo, J. Nutr. Food Sci. 5 (2014) 334, https://doi.org/10.4172/2155-9600.1000334.

[16] M. Mariño, L. Lopes da Silva, N. Durán, L. Tasic, Enhanced materials from nature: nanocellulose from citrus waste, Molecules 20 (2015) 5908–5923, https://doi.org/10.3390/molecules20045908.

[17] M.A. Mariño, C.A. Rezende, L. Tasic, A multistep mild process for preparation of nanocellulose from orange bagasse, Cellulose 25 (2018) 5739–5750, https://doi.org/10.1007/s10570-018-1977-y.

[18] S. Jongaroontaprangsee, N. Chiewchan, S. Devahastin, Production of nanocellulose from lime residues using chemical-free technology, Mater. Today Proc. 5 (2018) 11095–11100, https://doi.org/10.1016/j.matpr.2018.01.027.

[19] E.M. de Melo, J.H. Clark, A.S. Matharu, The Hy-MASS concept: hydrothermal microwave assisted selective scissoring of cellulose for in situ production of (meso) porous nanocellulose fibrils and crystals, Green Chem. 19 (2017) 3408–3417, https://doi.org/10.1039/c7gc01378g.

[20] A. Scurria, L. Albanese, M. Pagliaro, F. Zabini, F. Giordano, F. Meneguzzo, R. Ciriminna, CytroCell: valued cellulose from citrus processing waste, Molecules 26 (2021) 596, https://doi.org/10.3390/molecules26030596.

[21] D. Nuzzo, L. Cristaldi, M. Sciortino, L. Albanese, A. Scurria, F. Zabini, C. Lino, M. Pagliaro, F. Meneguzzo, M. Di Carlo, R. Ciriminna, Exceptional antioxidant, non-cytotoxic activity of integral lemon pectin from hydrodynamic cavitation, ChemistrySelect 5 (2020) 5066–5071, https://doi.org/10.1002/slct.202000375.

[22] S. Al Jitan, A. Scurria, L. Albanese, M. Pagliaro, F. Meneguzzo, F. Zabini, R. Al Sakkaf, A. Yusuf, G. Palmisano, R. Ciriminna, Micronized cellulose from citrus processing waste using water and electricity only, Int. J. Biol. Macromol. 204 (2022) 587–592, https://doi.org/10.1016/j.ijbiomac.2022.02.042.

[23] T. Endo, quoted in: Thinky, User Interview – Dr. Takashi Endo, National Institute of Advanced Industrial Science and Technology. Thinky Library. www.thinkymixer.com/en-gl/library/interview/user-interview-dr-takashi-endo-national-institute-of-advanced-industrial-science-and-technology/, November 1, 2017 (accessed on August 5, 2024).

[24] S.L. Waaijers-van der Loop, Z. Dang, E. Rorije, N. Janssen, Toxicity Screening of Potential Bio-based Polar Aprotic Solvents (PAS), National Institute for Health and Environment (RIVM), Den Hague, The Netherlands, 2018.

[25] E. Fontananova, R. Ciriminna, D. Talarico, F. Galiano, A. Figoli, G. Di Profio, R. Mancuso, B. Gabriele, G. Angellotti, G. Li Petri, F. Meneguzzo, M. Pagliaro, CytroCell@PIL: a new Citrus nanocellulose-polymeric ionic liquid composite for enhanced anion exchange membrane alkaline water electrolysis, ChemRxiv, 2024, https://doi.org/10.26434/chemrxiv-2024-q0xtq.

[26] K.M. Håkansson, A.B. Fall, F. Lundell, S. Yu, C. Krywka, S.V. Roth, G. Santoro, M. Kvick, L. Prahl Wittberg, L. Wågberg, Hydrodynamic alignment and assembly of nanofibrils resulting in strong cellulose filaments, Nat. Commun. 5 (2014) 4018, https://doi.org/10.1038/ncomms5018.

[27] H.-Y. Yu, H. Zhang, M.-L. Song, Y. Zhou, J. Yao, Q.-Q. Ni, From cellulose nanospheres, nanorods to nanofibers: various aspect ratio induced nucleation/reinforcing effects on polylactic acid for robust-barrier food packaging, ACS Appl. Mater. Interfaces 9 (2017) 43920–43938, https://doi.org/10.1021/acsami.7b09102.

[28] G. Siqueira, J. Bras, A. Dufresne, Cellulosic bionanocomposites: a review of preparation, properties and applications, Polymers 2 (2010) 728–765, https://doi.org/10.3390/polym2040728.

[29] K.-Y. Lee, Y. Aitomäki, L.A. Berglund, K.A. Oksman, A. Bismarck, On the use of nanocellulose as reinforcement in polymer matrix composites, Compos. Sci. Technol. 105 (2014) 15–27, https://doi.org/10.1016/j.compscitech.2014.08.032.

[30] (a) S. Spange, K. Fischer, S. Prause, T. Heinze, Empirical polarity parameters of celluloses and related materials, Cellulose 10 (2003) 201–212, https://doi.org/10.1023/A:1025197520736;
(b) C. Olsson, G. Westman, Direct dissolution of cellulose: background, means and applications, in: T.G.M. van De Ven, L. Godbout (Eds.), Cellulose - Fundamental Aspects, Intech, London, 2023, p. 143, doi:10.5772/52144.

[31] B. Lindman, G. Karlström, L. Stigsson, On the mechanism of dissolution of cellulose, J. Mol. Liq. 156 (2010) 76–81, https://doi.org/10.1016/j.molliq.2010.04.016.

[32] S. Naz, N. Ahmad, J. Akhtar, N.M. Ahmad, A. Ali, M. Zia, Management of citrus waste by switching in the production of nanocellulose, IET Nanobiotechnol. 10 (2016) 395–399, https://doi.org/10.1049/iet-nbt.2015.0116.

[33] P.M. Ejikeme, Investigation of the physicochemical properties of microcrystalline cellulose from agricultural wastes I: orange mesocarp, Cellulose 15 (2008) 141–147, https://doi.org/10.1007/s10570-007-9147-7.

[34] I. Bicu, F. Mustata, Optimization of isolation of cellulose from orange peel using sodium hydroxide and chelating agents, Carbohydr. Polym. 98 (2013) 341–348, https://doi.org/10.1016/j.carbpol.2013.06.009.

[35] Y. Liu, A. Liu, S.A. Ibrahim, H. Yang, W. Huang, Isolation and characterization of microcrystalline cellulose from pomelo peel, Int. J. Biol. Macromol. 111 (2018) 717–721, https://doi.org/10.1016/j.ijbiomac.2018.01.098.

[36] H. Dai, Y. Chen, L. Ma, Y. Zhang, B. Cui, Direct regeneration of hydrogels based on lemon peel and its isolated microcrystalline cellulose: characterization and application for methylene blue adsorption, Int. J. Biol. Macromol. 191 (2021) 129–138, https://doi.org/10.1016/j.ijbiomac.2021.09.063.

[37] M. Palaniappan, S. Palanisamy, R. Khan, N.H. Alrasheedi, S. Tadepalli, T. m. Murugesan, C. Santulli, Synthesis and suitability characterization of microcrystalline cellulose from *Citrus x sinensis* sweet orange peel fruit waste-based biomass for polymer composite applications, J. Polym. Res. 31 (2024) 105, https://doi.org/10.1007/s10965-024-03946-0.

[38] C. He, H. Li, O. Huan, H. Wei, H. Xiong, H. Ni, M. Zheng, Physicochemical properties and structure characterization of microcrystalline cellulose from pomelo fruitlets, J. Food Process. Preserv. 46 (2022) e17071, https://doi.org/10.1111/jfpp.17071.

[39] B. Rivas, A. Torrado, P. Torre, A. Converti, J.M. Domínguez, Submerged citric acid fermentation on orange peel autohydrolysate, J. Agric. Food Chem. 56 (2008) 2380–2387, https://doi.org/10.1021/jf073388r.

[40] J. Lin, cit. in: Evera, Citrosuco launches unit for natural ingredients production for different industries, PR Newswire. https://www.prnewswire.com/news-releases/citrosuco-launches-unit-for-natural-ingredients-production-for-different-industries-301685274.html, 22 November 2022 (accessed on April 12, 2024).

[41] Evera, Evera Fiberfel Brochure, See at: https://www.everaingredients.store/documents/515260, 2024 (accessed on April 12, 2024).

[42] Vitacyclix, Citrus Pectin Cellulose, See at: https://www.ulprospector.com/en/na/Food/Detail/15885/2402881/Citrus-Pectin-Cellulose, 2024 (accessed on April 12, 2024).

[43] LBG Sicilia, Citrifiber, See at, https://lbg.it/product/citrifiber/, 2024 (accessed on April 12, 2024).

[44] K.M. Vanhatalo, K.E. Parviainen, O.P. Dahl, Techno-economic analysis of simplified microcrystalline cellulose process, BioRes 9 (2014) 4741–4755, in: https://bioresources.cnr.ncsu.edu/resources/techno-economic-analysis-of-simplified-microcrystalline-cellulose-process/ (accessed on August 5, 2024).

[45] Yarrow Chem Products, Price List - June 2023. Mumbai. https://yarrowpharm.com/wp-content/uploads/2023/06/YARROW-PRICE-LIST-JUNE-2023.pdf, 2023 (accessed on April 12, 2024).

[46] R. Boetzel, J. Schlingemann, S. Hickert, C. Korn, G. Kocks, B. Luck, G. Blom, M. Harrison, M. François, L. Allain, Y. Wu, Y. Bousraf, A nitrite excipient database: a useful tool to support *N*-nitrosamine risk assessments for drug products, J. Pharm. Sci. 112 (2023) 1615–1624, https://doi.org/10.1016/j.xphs.2022.04.016.

[47] The Business Research Company, Orange Juice Global Market Report 2024. London. https://www.thebusinessresearchcompany.com/report/orange-juice-global-market-report, 2024 (accessed on April 10, 2024).

[48] M.F. Neves, V.G. Trombin, V.N. Marques, L.F. Martinez, Global orange juice market: a 16-year summary and opportunities for creating value, Trop. Plant Pathol. 45 (2020) 166–174, https://doi.org/10.1007/s40858-020-00378-1.

[49] S. Yoon, M. Zansler, L. House, Inflation in Orange Juice Prices and Consumer Responses, FE1142, 2/2024. EDIS 2024 (1). Gainesville (FL), 2024, https://doi.org/10.32473/edis-FE1142-2024.

[50] M. Pagliaro, An industry in transition: the chemical industry and the megatrends driving its forthcoming transformation, Angew. Chem. Int. Ed. 58 (2019) 11154–11159, https://doi.org/10.1002/anie.201905032.

[51] R. Ciriminna, M. Ghahremani, B. Karimi, M. Pagliaro, Emerging green routes to nanocellulose, Biofuels Bioprod. Biorefin. 17 (2023) 10–17, https://doi.org/10.1002/bbb.2423.

[52] J. Pennells, I.D. Godwin, N. Amiralian, D.J. Martin, Trends in the production of cellulose nanofibers from non-wood sources, Cellulose 27 (2020) 575–593, https://doi.org/10.1007/s10570-019-02828-9.

[53] R. Ciriminna, G. Angellotti, G. Li Petri, F. Meneguzzo, C. Riccucci, G. Di Carlo, M. Pagliaro, Cavitation as a zero-waste circular economy process to convert citrus processing waste into biopolymers in high demand, J. Bioresour. Bioprod. (2024), https://doi.org/10.1016/j.jobab.2024.09.002.

[54] A. Chaker, S. Alila, P. Mutje, M. Rei, S. Vilar, S. Boufi, Key role of the hemicellulose content and the cell morphology on the nanofibrillation effectiveness of cellulose pulps, Cellulose 20 (2013) 2863–2875, https://doi.org/10.1007/s10570-013-0036-y.

[55] J. Zhang, J. Wu, J. Yu, X. Zhang, J. He, J. Zhang, Application of ionic liquids for dissolving cellulose and fabricating cellulose-based materials: state of the art and future trends, Mater. Chem. Front. 1 (2017) 1273–1290, https://doi.org/10.1039/c6qm00348f.

[56] Biobased Markets, The Directory of Cellulose Nanomaterials. https://tappinano.org/media/1649/the-directory-of-cellulose-nanomaterials-may-19-2023.pdf, 2023. (Accessed 5 August 2024).

[57] R. Ciriminna, G. Angellotti, R. Luque, M. Pagliaro, Green chemistry and the bioeconomy: a necessary nexus, Biofuels Bioprod. Biorefin. 18 (2024) 347–355, https://doi.org/10.1002/bbb.2585.