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Abstract

Skin biocompatible materials are amongst the fastest-growing markets for nanocelluloses, with a growing number of patents published over the past ten years. This review highlights the recent developments, market trends, safety assessment, safety regulations, and challenges for different nanocellulose types used in skincare, cosmetics, and healthcare. Firstly, different classes of nanocelluloses (nanoparticles, nanocrystals, nanofibers, nanoyarns, hydrogels) and their synthesis methods were highlighted. Secondly, unique properties of nanocelluloses for applications onto the skin (i.e. high surface functionality, high dispersion stability, high water-holding capacity, and biocompatibility) were highlighted. Thirdly, recent uses of nanocellulose composite as carriers for bioactive compounds and UV-blockers as well as wound healing and skin sensors were also provided. Finally, a toxicological assessment for various nanocellulose types was discussed based on their sizes and morphologies. The challenges and perspectives for an industrial breakthrough are related to further optimization of production and processing conditions of nanocelluloses were also highlighted.

Keywords: Spherical Cellulose Nanoparticles; Cellulose Nanocrystals; Cellulose Nanofibers; Bacterial Cellulose; Cellulose Nanoyarn; Cellulose Hydrogels; Wearable Sensors; Skin Regeneration

1. Introduction

Over the past decades, nanocelluloses have dramatically evolved as highly functional and biocompatible materials for applications onto the skin e.g. skincare, cosmetics, healthcare and health monitoring (Mohiuddin, 2019). A new class of wearable sensors so called as lab-on-skin where smart, flexible and stretchable devices are integrated into the skin, provides direct monitoring and diagnostic interfaces to the body. Skincare formulations (makeup, creams, lotions, facemask) are generally created by combining chemical compounds from synthetic or natural sources (Banerjee, 1988). Thickening agents, film formers, ultraviolet absorbents, antioxidants, sequestering agents, coloring agents, vitamins, pharmaceutical agents are the main components in many cosmetics and skincare formulations (Herman et al., 2012). The oily materials (e.g., oils, fats, waxes, and ester oils, and surface-active agents, emulsifiers, solubilizing agents, higher alcohols, fatty acids, and silicones) further control the evaporation of moisture from the skin and improve the sensitive feeling (Santos et al., 2019). Natural and synthetics polymers are key ingredients in products for hair care (shampoos, tip repair, conditioners, hair dyes, fixing gels, moisturizing masks), skincare (liquid soaps, body oils, moisturizing lotions, sunscreen), and appearance improvement (nail care, fragrance, make-up). Nowadays, industrial investments are growing in the development of “green-tech” solutions replacing synthetic ingredients with natural materials. New skincare, cosmetics, health monitoring products include natural biopolymers and bioactive compounds to meet the high demands for therapeutic and protective care products, which stimulate the skin functions such as healing, protection, immunity and thermoregulation (Aguilar-Toalá et al., 2019). The proteins (e.g., collagen and wheat proteins) and polysaccharides (e.g., cellulose, alginic acid, and hyaluronic acid) have been particularly added to enhance specific functionalities of the products applied onto the skin.

Nanocelluloses (nanoparticles, nanocrystals, nanofibers, nanoyarns, and bacterial cellulose) have been recently integrated into skincare, cosmetics, and health monitoring products as green alternative biopolymers to replace synthetic polymers such as polyethylene, polyacrylamides, and nylon (Almeida et al., 2021). The nanocelluloses are primarily produced from soft and hardwood species, phloem fibers (flax, hemp, jute, ramie), grasses (bagasse, bamboo); or non-pathogenic bacteria, fungi, algae, and marine animals (Sfiligoj et al., 2013). The nanocelluloses are promising sustainable nanomaterials for skincare formulations with enhanced performance, owing to their biocompatibility, high aspect ratio, high surface area, abundant surface charge, and mechanical strength. In addition, the surface chemistry of nanocelluloses can be easily modified for tuning affinity towards specific bioactive molecules and drugs (Thomas et al., 2018). At present, the global nanocelluloses market is forecasted to achieve USD 783 million by 2025, with an expected annual market growth rate of 21.4% from 2020 to 2026 (Trache et al., 2020). To date, nanocelluloses have been used as anti-wrinkle agents, compatibilizers, moisturizers, and rheological agents or thickeners. They have been added in cleansing formulations to remove dirt, reduce sebum and exogenous contaminants, and control skin odor and microflora (Mishra et al., 2020). Especially nanocellulose hydrogels show great promise in a range of skincare and healthcare applications. They provide a thick but non-tacky feel and are especially applied as an additive in mask packs and basic cosmetics. Nanocellulose hydrogels retain high water content and this keeps the wound warm and moist, which is optimal for healing. They have been also used for in developing novel wearable biosensors that able to monitor biomarkers levels for disease diagnosis and health monitoring (Dervisevic et al., 2020).

This review discusses recent advances in nanocelluloses in the framework of skin biocompatible materials, as well as their formulations, composition and functionality as well as their emerging skincare applications. The roles of different nanocellulose types (spherical nanoparticles, nanowhiskers or nanocrystals, nanofibers, nanoyarns, hydrogels, bacterial cellulose) and their exceptional properties for application in cosmetics, skincare, skin regeneration, wound healing, and skin wearable sensors are presented. This multidisciplinary article also offers an updated and critical assessment of recent findings on uses of nanocelluloses as thickeners, anti-wrinkle agents, compatibilizers, moisturizers, film-forming materials, formulation modifiers, UV-blockers, and drug delivery vehicles. Both relevant scientific research topics and industrial patents on nanocelluloses in skincare and cosmetics are comprehensively summarized. A perspective on nanocelluloses used in skincare formulations is given concerning current safety regulations. The challenges for fast progress in commercial application and future perspectives of nanocelluloses for applications onto the skincare are finally covered.

2. Origins and production of nanocelluloses

Nanocellulose is obtained as an engineered product from cellulose, which occurs as the most abundant material in plant cell walls with an intrinsic hierarchical nanostructure. The chemical structure and number of repeating cellobiose units in the cellulose structure determine the polymerization degree. The functional groups (hydroxyl groups) at the outer sites give rise to strong intermolecular hydrogen bonds forming a network with parallel sheet-like molecular stacking and supramolecular ordering. The morphologies and characteristics of nanocellulose (size, morphology, aspect ratio, surface charge, functionality) can be modulated by selecting specific raw materials, fabrication techniques, and processing parameters. According to their length, diameter, aspect ratio, and composition, the nanocelluloses can be classified as in Table 1 (Barhoum et al., 2020), with: *(i)* nanocellulose spherical particles (NCSPs; amorphous and crystalline), *(ii)* cellulose nanocrystals (CNCs, crystalline), *(iii)* cellulose nanofibrils (CNFs, semi-crystalline), or *(iv)* bacterial cellulose (BNC, higher crystallinity), and *(iv)* cellulose nanoyarns (CNY, semi-crystalline). A description of the different nanocellulose morphologies is best illustrated with microscopic images in Figure 1.

Table 1. Nomenclature, size, morphology, and preparation methods of cellulose nanomaterials

Nanocellulose type	**Size range**	**Morphology**	**Crystallinity**	**Sources and preparation**	**Ref**
Nanocellulose spherical particles (NCSP)	Diameter: 50-100 nm	Spherical	Amorphous or semi-crystalline	Waste cotton through mild enzymatic hydrolysis	(Meyabadi et al., 2014)
Cellulose nanocrystal (CNC)	Length: 100 nm–1 µm	Rod-like	Crystalline	Alkali treatment and acid hydrolysis of	(Heath & Thielemans, 2010)
Cellulose nanofibril (CNF)	Length: 1 –3 µm Diameter:	Fibers with network structures	Semi-crystalline	Mechanical treatment (refining) of wood or	(Barhoum et al., 2020)

Bacterial nanocellulose (BNC)	Length: 200 nm–3 µm Diameter:	Fibers with network structures	Highly crystalline	Biological treatment of cellulose-based materials	(Boisset et al., 2000)
Cellulose nanoyarn (CNY)	Length: several microns Diameter:	Fibers with network structures or aligned structures	semi-crystalline	Electrospinning of cellulose derivative with a	(Gouda et al., 2014)

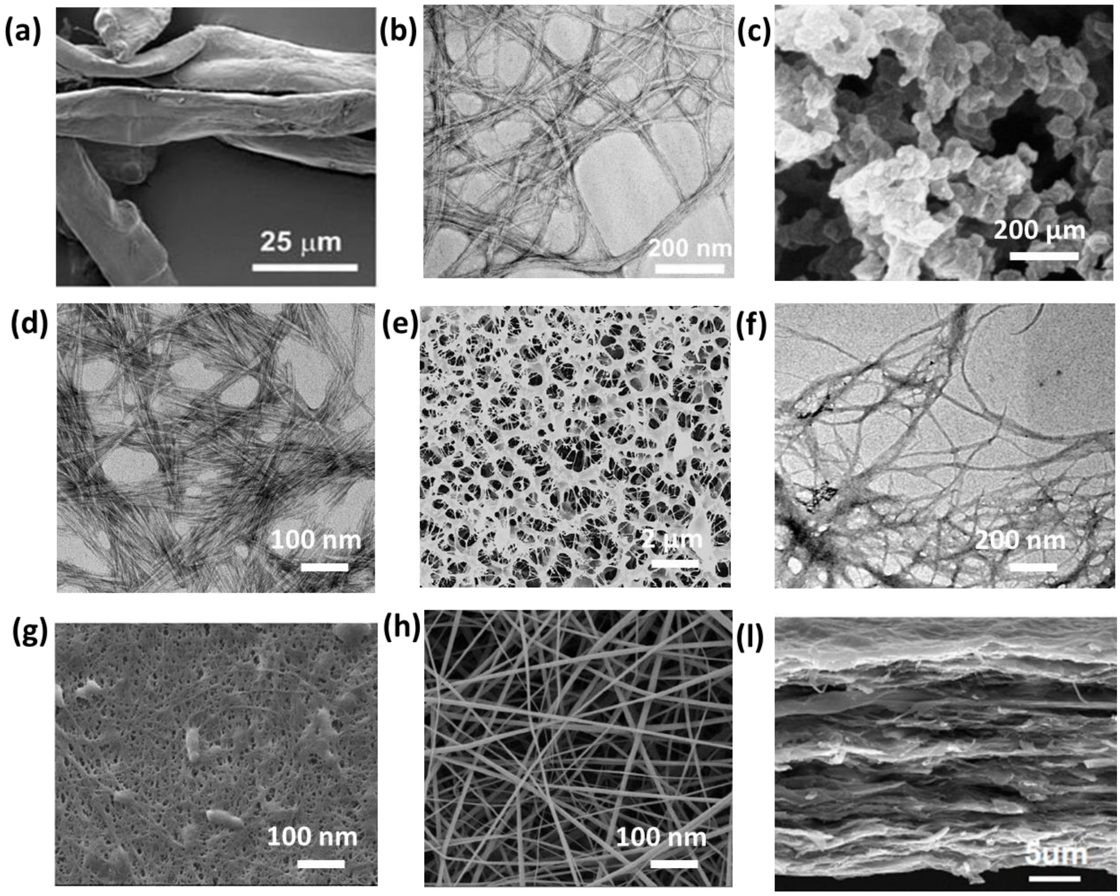
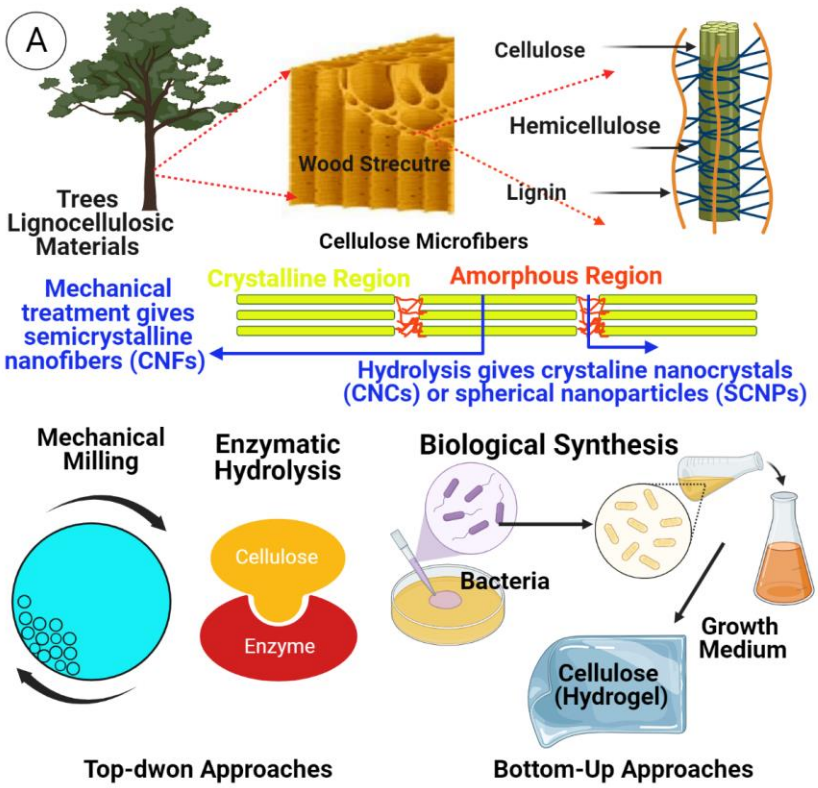


Figure 1. Different size and morphologies of cellulose-based materials observed by scanning electron microscopy (SEM) or transmission electron microscopy (TEM): (a) cellulose microfibers (CMFs) from wood pulp (Gentile et al., 2018); (b) cellulose nanofibers (CNFs) from wood pulp (Nissilä et al., 2021); (c) spherical cellulose nanoparticles (NCSPs) from plant sources (Zhang et al., 2007); (d) cellulose nanocrystals (CNCs) from plant source (J. Dai et al., 2018); (e) hydrogel prepared from cellulose nanocrystals (Zhang et al., 2017); (f)

cellulose nanofibers (CNFs) from plant origin (Yassin et al., 2019); (g) bacterial nanocellulose (BNC) (Orlando et al., 2020); (h) cellulose nanoyarns (CNYs) by electrospinning from cellulose acetate (Rodríguez et al., 2014); (i) cross-section of cellulose film prepared from cellulose nanofibers (Qi et al., 2020).

To date, the main raw materials to obtain nanocelluloses are plants, whereas bacteria and microalgae, tunicates are currently less used (Barhoum et al., 2020). The selected plant fibers for the production of cellulose can be distinguished according to six main clusters, i.e. bast, core, grass and reed, leaf, seed, or other fibers. Wood pulp fibers or residual paper fibers are common sources for conversion into nanocellulose due to the relatively high purity of cellulose after bleaching, their ductility, and excellent physical properties (Barhoum et al., 2020). Using the proper combination of mechanical, chemical, physicochemical, and/or biological processing steps, both length and diameter of native cellulose microfibers can be progressively reduced to create cellulose substances with at least one dimension in the 10-100 nm range. Researchers have currently developed several processing routes for nanocellulose fabrication (Zhang et al., 2019), as schematically illustrated in Figure 2: *(i)* mechanical routes, including milling, grinding, refining, homogenization, cryo-crushing normally require high-energy input and provide a high yield of low-crystalline nanocelluloses (CNF) at relatively low cost; *(ii)* physical routes, including ultrasonication, steam explosion, wet spinning, dry spinning, melt spinning, electrospinning, and 3D printing have been used to produce electrospun cellulose acetate nanofiber (Barhoum et al., 2019), (Long et al., 2019); *(iii)* chemical routes, including alkali treatment, followed by acid hydrolysis with appropriate chemicals and optimized reaction conditions generally provide highly crystalline nanocelluloses (CNCs) with specific functionalities and high purity (Barhoum et al., 2019); *(iv)* biological routes, including enzymatic hydrolysis are typically combined with mechanical fragmentation or chemical hydrolysis to reduce chemical waste and energy consumption. Bacterial nanocellulose (BNC) is naturally produced as an exopolysaccharide by some bacteria (former *Gluconacetobacter*) cultivated in a medium with carbon and nitrogen sources (Rasouli et al., 2019). Unlike nanocelluloses produced by former methods, BNC is free of lignin, hemicelluloses, and pectin. Similarly, microalgae are a largely unexplored source of new forms of nanocellulose. Microalgae can be grown in ocean-based systems or on non-arable land using salt- or wastewater (Ross et al., 2021). Tunic tissue of tunicates (marine invertebrate animals) is the only known animal source of crystalline nanocelluloses (Zhang et al., 2019).



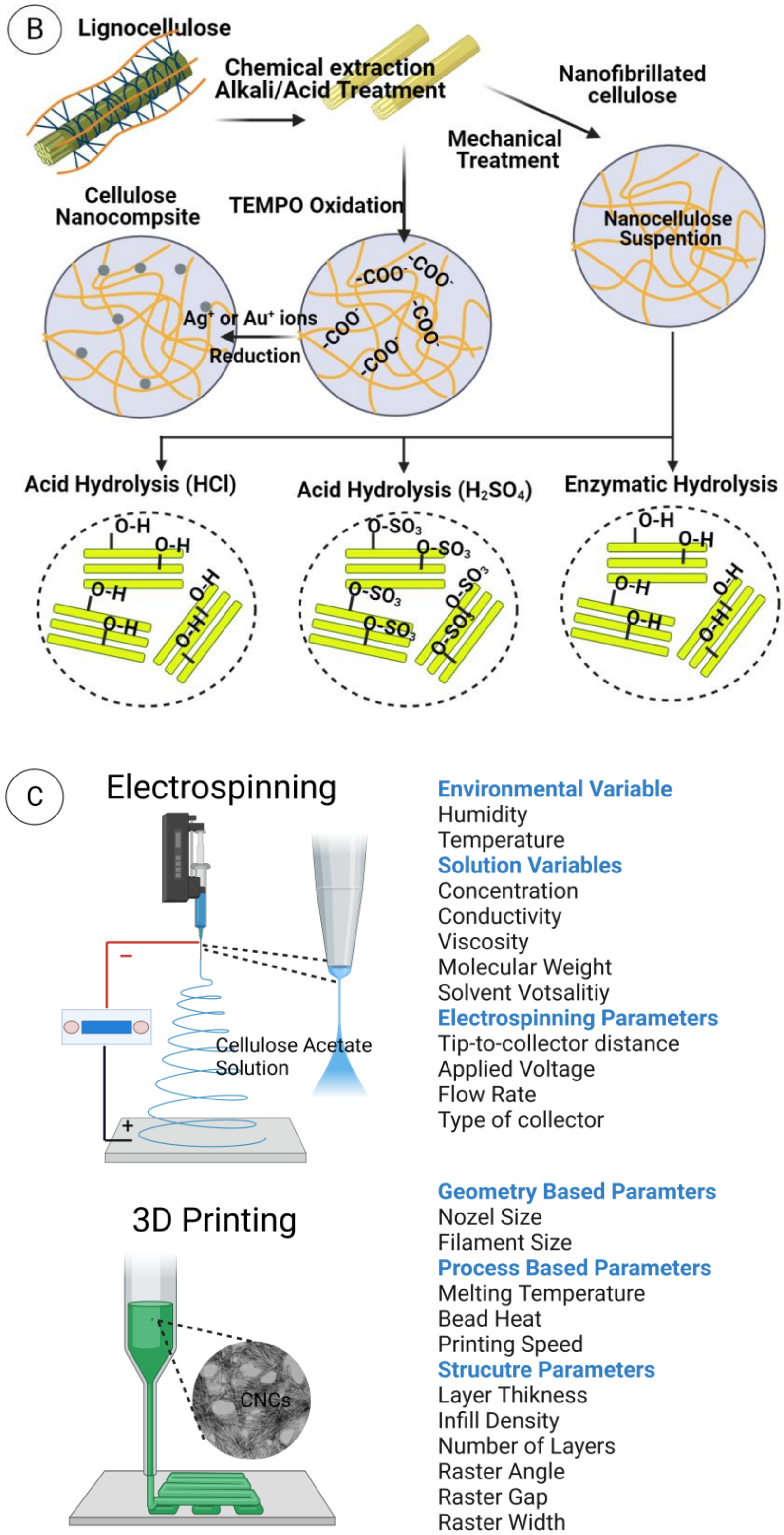


Figure 2. A schematic presentation summarizes different routes for synthesis and surface functionalization of nanocelluloses: (a) Mechanical (ball milling) and biological routes (enzymatic hydrolysis and bacterial synthesis) for producing nanocelluloses; (b) chemical

routs for producing nanocelluloses from bacteria followed by chemical functionalization from plant sources; (c) physical routes for fabrication of nanocelluloses electrospinning and 3D printing process and their processing parameters.

Size, morphology, crystallinity, and surface chemistry among other properties of nanocelluloses, vary with their origin and processing protocols. Thus, it offers a toolbox set to adapt desired features towards a given application while it is challenging to produce nanocelluloses with predetermined and constant properties. After the discovery of nanocellulose in the early 1980s, the initial commercialization was limited by the high energy requirements (≅ 30,000 kWh/ton) for fiber disintegration during mechanical production (Barhoum et al., 2019). However, recent progress in energy-saving pretreatments of cellulose fibers has reduced the energy requirements by more than 98% (Zhang et al., 2019). Consequently, the first industrial pilot-scale factories for CNCs and CNFs production were established from 2012 on with increasing capacities. The global market size of nanocelluloses turns close to USD 146.7 million in 2019 and is expected to grow at an annual rate of 21.4% from 2020 to 2026 (Katz et al., 2015). Figure 3 depicts the market distribution of nanocellulose and its use in specific niche segments (Kiral Puldini, 2020). Although the market share of nanocellulose in skincare, cosmetics, health monitoring products is relatively small, this is expected to be the most expanding domain in coming years particularly for sunscreen lotions, creams and novel cosmeceuticals (Kiran Pulidindi, 2020), (Blanco et al., 2018).

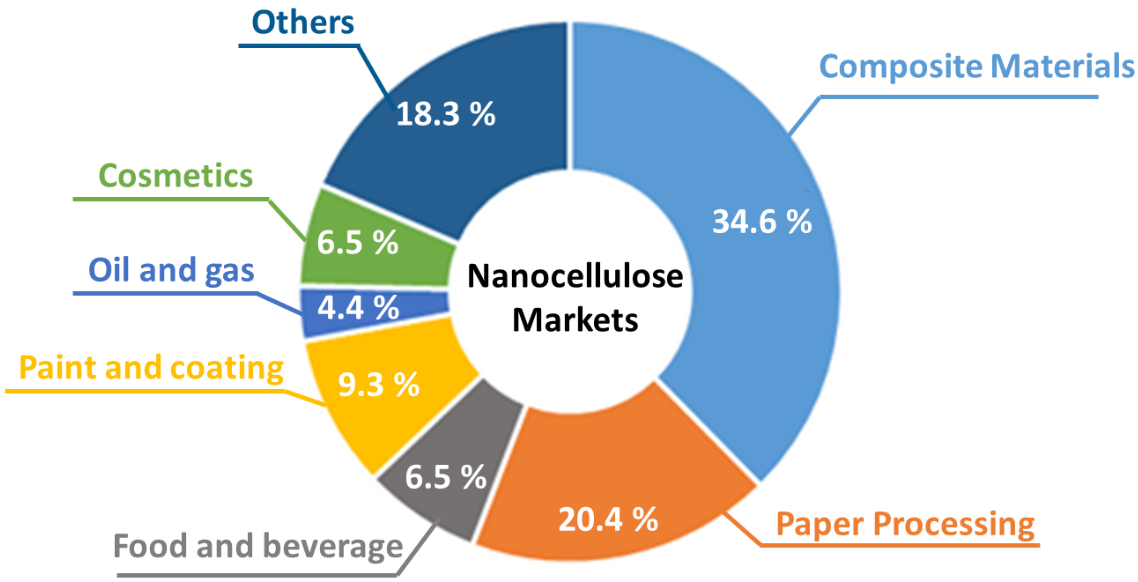


Figure 3. Market share of nanocellulose products with the contribution in different segments with 6.5 % in cosmetics and personal care products.

3. Unique properties of nanocellulose for application onto skin

Some nanocelluloses properties are superior comparing to those of the native cellulose, thanks to their high surface reactivity and ability for formation of a dense network structure with high intrinsic strength and high stiffness along the single fibers (Blanco et al., 2018; De Amorim et al., 2020). The high specific surface area occupied by hydroxyl side groups (-OH) and large water holding capacity provide the nanocellulose materials with interesting features for skincare, cosmetics, health monitoring products.

3.1 High surface functionality

Nanocelluloses, like many other polysaccharides, have a surface with plenty of hydroxyl moieties that are available for chemical modification or become easily hydrated, thus increasing the compatibility with biological tissue. The surface modification of nanocelluloses can be classified into three groups: *(i)* native surface chemistry during the isolation/purification process or as a result of similar methods of surface treatment, *(ii)* physical adsorption at the surface through electrostatic charge interactions, and *(iii)* covalent bond formation or derivatization (Tortorella et al., 2020). The chemical modifications are mainly performed to introduce charged or hydrophobic moieties through amination, esterification, oxidation, silylation, carboxymethylation, epoxidation, sulfonation, thiol- and azido-functional reactions (Vecino et al., 2017). Recently, nanocelluloses have been produced by grafting side groups near the hydroxyl groups at positions C2, C3, or C6 of the glucopyranose monomer. The chemical stability, salt tolerance and acid resistance of modified nanocelluloses are thus improved compared with native nanocellulose. The aqueous media with modified nanocellulose display higher viscosity, pseudo-plasticity, and thixotropy when added at high concentrations to suspensions and emulsions, increasing the gel strength and thickening performance (Barhoum et al., 2019). The high surface area and functionalization capacity make nanocelluloses suitable as thickeners, emulsifying agents, wetting agents, foaming substances, and hydrating and/or moisturizing agents to enhance skin perception (Mellou et al., 2019).

3.2 High viscosity and shear thinning behavior

Nanocellulose has interesting rheological features resulting in good applicability and skin feel. As an additive in skincare and cosmetic formulations, it regulates the rheological features for viscosity, thickening, and film formation, allowing to adapt the performance and physical properties of personal care products (Mitura et al., 2020; Alves et al., 2020). The rheological properties are mainly governed by the morphology, concentration, and degree of substitution of the nanocellulose. The good applicability of nanocellulose in creams and lotions is explained by its intrinsic viscous-elastic properties. In particular, the high viscosity at zero shears reduces the dripping effect and the intrinsic shear-thinning effect facilitates the spraying application (Tortorella et al., 2020). The gelling properties with high gel strength are attributed to the formation of chemical cross-links between carboxyl groups, forming a three-dimensional network structure. In parallel, the gel network retains water inside and can be exploited to improve the water retention of the final product. Unlike other rheological modifiers, the thickening and film-forming properties of nanocelluloses allow the formation of a thick layer by only one spray application. The thickening features make them suitable for sunscreen sprays. After application and drying, they provide a homogeneous layer with a non-oily skin appearance having a smooth haptic feeling on the body and face (Dufresne, 2019). Nanocelluloses have been used as slipping agents to enhance the cream's smooth texture, as an anti-caking agent for skincare and cosmetic foundations, and as film former for thin-layer nail polishes. By tuning the rheological and iridescence features of the dispersions, a nanocellulose thickener is compatible with cosmetic products for eyelashes, hair, nails, and eyebrows, among pharmaceutical products (Dhali et al., 2021).

3.3 High dispersion stability over a wide pH range

Nanocelluloses possess long shelf life and provide aqueous dispersions with enhanced stability at a broad pH range and high temperatures. The formulations of skincare emulsions and suspension can benefit from better stability and homogeneous mixing of its components in aqueous media. Nanocelluloses are used in skincare formulations to stabilize oil-in-water emulsions without the need for additional surfactants. Unmodified pristine nanocelluloses with high surface charge density are not effective stabilizers for oil-in-water emulsions (Lin et al., 2019). The nanocelluloses with grafted hydrophobic polymers such as cinnamoyl chloride or butyryl chloride can enhance their affinity towards the oil phase, thus reducing the interfacial tension. The hydrophobic nanocelluloses are therefore increasingly used as a natural stabilized for Pickering emulsions. Depending on the increase in the aspect ratio of different CNCs morphologies, the different stabilization mechanisms of nanocellulose in emulsions are illustrated in **Figure 4a** (Tang et al., 2019)**.** The CNCs with increasing aspect ratio could be obtained through acid hydrolysis of various sources including cotton (low aspect ratio), BNC (intermediate aspect ratio), and Cladaphora green algae (high aspect ratio) (Kalashnikova et al., 2013). The nanocellulose emulsions have better stability upon changes in pH, temperature, and salt concentrations compared with gum-based formulations (Ullah et al., 2016).

3.4 High water-holding and retention capacity

Nanocellulose has a high water-holding capacity with a water content of up to 80% and consequently has a gel-like appearance even at rather low concentrations. The high water holding capacity or water retention is particularly mentioned as a key property of a dense fibrillary nanocellulose network (CNF), where the free water is entrapped and not easily released (Tortorella et al., 2020). Although nanocelluloses display excellent water-holding capacity, they are not water absorbents and not soluble in water (Lin et al., 2019). Therefore, nanocellulose can preserve the moisturizing effect on the skin and enhance wet compatibility with skin and hair. The nanocellulose can be dispersed in strong polar solvents (especially water) due to the strong interaction between the surface hydroxyls or carboxyl group and their gelation mechanism can be tuned by changing the nanocellulose concentration, varying pH of the medium, adding salt, or crosslinking (**Figure 4b**) (Mendoza et al., 2018). As drying of nanocellulose is an irreversible process, it cannot be easily redispersed and does not re-absorb the same amount of water. The drying process introduces agglomeration that reduces the surface area and changes the surface character permanently. Relying on the water-holding properties, nanocellulose was industrially introduced in diapers and deodorant sheets, allowing the production of less fluffy material and thinner pads with high mechanical strength. Using the recently developed nanohydration technology, the nanocellulose is also contained in moisturizing masks with anti-aging features for the eye, face, or neck.

3.5 Purity and biocompatibility

Nanocellulose can be obtained with high purity and biocompatibility, which makes it reliable to use, while not affecting the smell and appearance of the final formulations. The source and processing route define the nanocellulose composition and possible impurities. When produced from plant (lignocellulosic) sources, the nanocelluloses contain different grades of hemicelluloses and lignin. However, these impurities can be removed using additional pretreatment steps such as chemical bleaching. Alternatively, the BNC is preferred as it is directly produced with extremely high purity and 100% cellulose content (Lin et al., 2019). Highly pure nanocelluloses for cosmetics are typically whitish and have a neutral appearance, thus avoiding the need to adjust the final formulations to obtain a constant color and appearance (Lin et al., 2019). Impurities might lead to incompatibilities or decrease the formulation performance due to interactions with other formulation ingredients. Impurities might also interact with the hydroxyl groups of nanocellulose, making them less available for proper interaction with the formulation ingredients. Impurities might also lead to allergies, unwanted effects or unexpected reactions (Blanco et al., 2018). High water retention capability, flexibility, biocompatibility, high purity, and high drug loading capacity make BC a potential material for wound healing applications.

3.6 Multifunctional nanocarriers

Nanocellulose hydrogels with nanoscale porosity offers the capacity to load bioactive ingredients and UV-blockers. The nanocellulose matrix protects the encapsulated ingredients as they will not react or decompose upon direct exposure to the environment or sunshine. The nanocelluloses themselves have no antimicrobial properties, but they can be added through loading with an antimicrobial agent (Kupnik et al., 2020). Recently, CNFs decorated with TiO_2 and ZnO nanoparticles having high refractive index and UV absorbance are used to produce transparent nanocellulose films (**Figure 4c**). The deposition of TiO_2 nanoparticles through physical interaction adds good UV resistance to nanocellulose fibers (Souto et al., 2020). The TiO_2 can be further modified with hydrophobic (γ-aminopropyl) triethoxysilane to obtain $–NH_2$ groups that can interact with the –OH groups of the CNF (Zhao et al., 2018). The high transparency of such hybrid films results in materials with excellent optical and mechanical features. Therefore, nanocellulose-based composites have a high potential for protective skincare formulations. As nanocellulose is odorless, it does not interfere with the selected fragrance added to a skincare product or it can serve as a carrier for the fragrance itself. Due to its intrinsic properties (biocompatibility, biodegradability, high surface area, unique rheological properties, and geometrical dimensions), nanocellulose is widely studied for drug delivery systems to the skin and oral routes. Its potential multifunctionality through chemical modification can be exploited to bind and release therapeutic agents and/or antibacterial compounds (Kupnik et al., 2020).

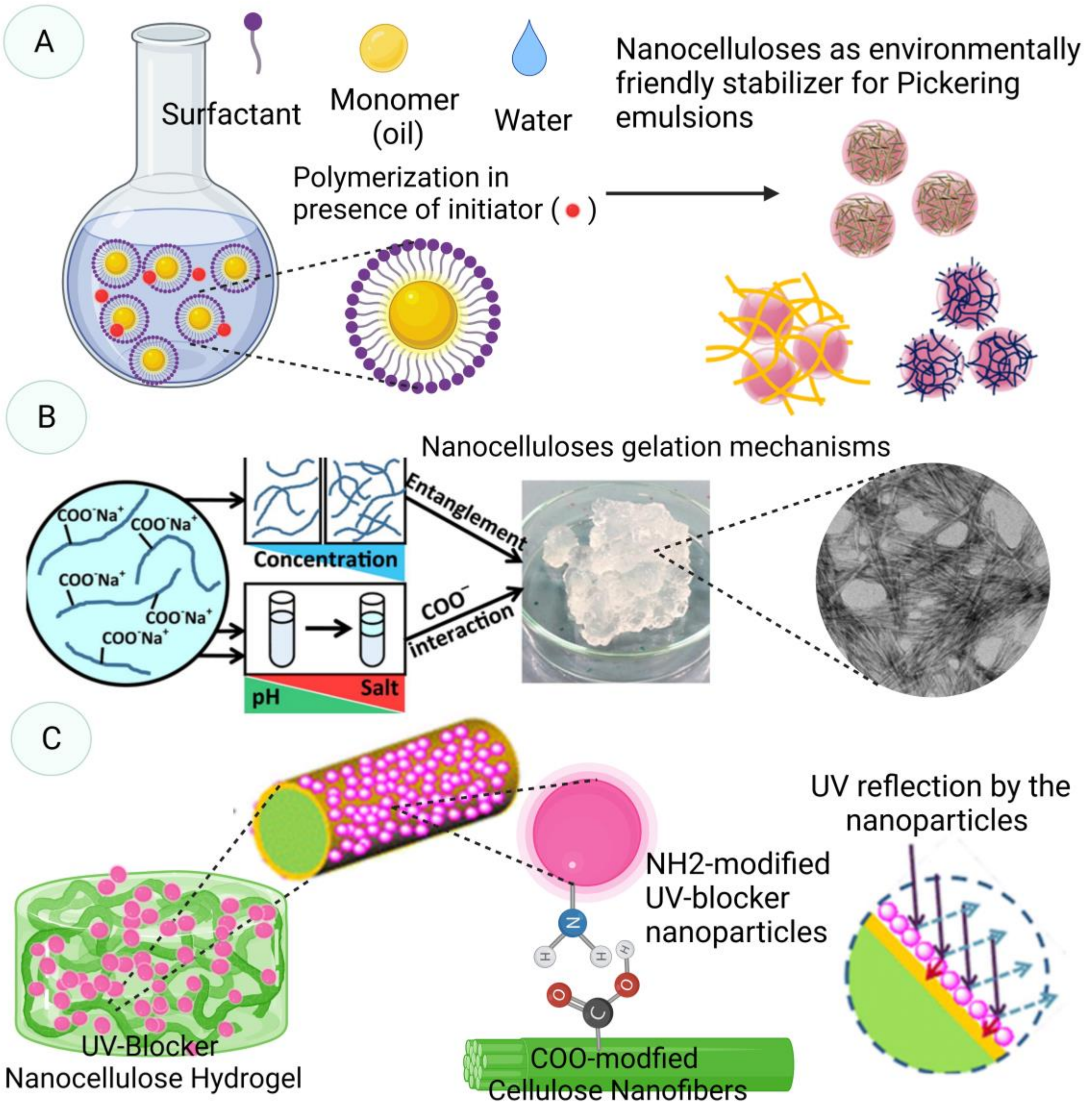


Figure 4. Unique characteristics of nanocelluloses for skincare formulations: (a) Nanocellulose satisfies the increasing demands for a sustainable and environmentally friendly stabilizer for Pickering emulsions with different aspect ratio to stabilize oil droplets. (b) Nanocelluloses have high ability for dispersion in some strong polar solvents (water) and gel formation mechanism can be controlled by changing the reaction parameters such as nanocellulose concentration, pH of the medium, or adding salt or cross-linker, Figure adapted from (Mendoza et al., 2018); and (c) Nanocellulose can be used as in production of a UV-resistant composite by adding inorganic UV-blocker nanoparticles with appropriate surface modification.

4. Application of nanocelluloses for cosmetics and skincare products

Emerging applications of nanocelluloses in cosmetics and skincare formulations are increasing because of their superior functionality, stability and long-lasting effects (Mihranyan et al., 2012). An overview of application domains of nanocelluloses in cosmetics and skincare formulations together with unique properties and surface functionalization during production is summarized in **Figure 5**. Initially, nanocelluloses were incorporated in cosmetics and skincare formulations as film-forming material to create a protective shield for the skin against harmful sunlight radiation (Kushwaha et al., 2020). New skincare products based on nano-emulsion systems use nanocellulose thickeners and stabilizers (Hameed et al., 2019; S. Singh et al., 2020), and they were also used as nanocarriers and delivery agents for active pharmaceutical ingredients (Hameed et al., 2019). To date, the personal care industry is expected to become the second-fast growing sector for the nanocellulose market. Among the leading companies commercializing medical-grade nanocelluloses, different grades were marketed as CNF hydrogels, wound dressing products or CNF/alginate bio-inks. The bio-inks have been used to fabricate human cartilage by co-culturing stem cells with chondrocytes in a hydrogel (X. Wang et al., 2020).

The nanocelluloses display many interesting features for the skincare and cosmetics industry, such as thickening, film-forming, bonding, dispersing, suspending, homogenization, emulsifying, gelling controlling, and stabilizing properties (Trache et al., 2020). Nanocelluloses also have a plasticizing effect and promote the formation of soft and elastic films with strong adhesion to protect the skin, therefore providing a lubricating function (Kukrety et al., 2018). Besides, chemical modification of nanocelluloses has been produced through modification of the hydroxyl groups to improve their solubility and compatibility. The robust humectant properties of nanocelluloses enhance the moisture quantity on the skin. Hence, nanocelluloses were added to moisturizing products, such as lotions, masks, and creams (Amnuaikit, 2011). For example, nanocelluloses such as CNFs and CNCs masks possess superior mechanical features compared with hydrogel masks, that facilitate their applications and handling (Sharma et al., 2018). Some recent applications of nanocellulose based materials and their advantages in different skincare and cosmetic products are summarized in **Table 2**. **Table 3** gives an overview of a patent summary and emerging industrial applications for different types of nanocelluloses in skincare and cosmetic applications. The specific utilization of the nanocellulose types in skincare and cosmetic applications is further detailed in next paragraphs.

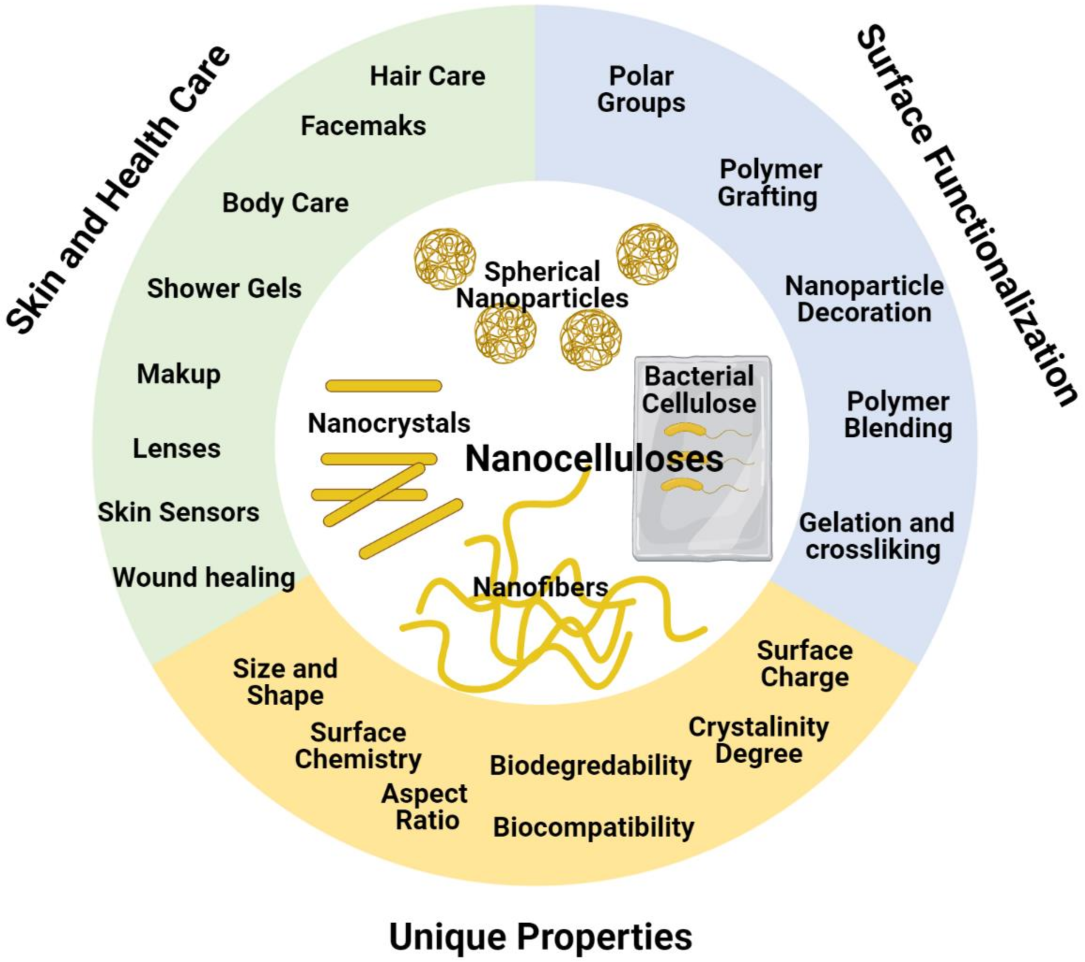


Figure 5. Different applications domains of nanocelluloses as ingredients for topical use in skincare, cosmetics, and healthcare products concerning their unique properties and functionalization.

Table 2. Potential use of nanocellulose as active ingredients and application domains in skincare and cosmetic products.

Products	Nanocellulose ingredient	Attributes	Function	Ref.
Sunscreen cream with UV filters function	Nanocellulose decorated with inorganic metal oxide nanoparticles (TiO_2 and ZnO)	- TiO_2 are UV-B filters - ZnO have a broad spectrum of activity (against UV-A and UV-B) - ZnO and TiO_2 provide optimal transparency	- Homogeneous distribu-tion of UV filters - Increased layer thickness - Non-dripping - Film formation - Water protection - Anti-wrinkling effect - Soft skin feeling effect - Cleansing effect	(Hameed et al., 2019; Kushwaha et al., 2020)
Body cream with antibacterial and antifungal agents	Nanocellulose decorated with Ag and Au nanoparticles	- Broad-spectrum activity - Superior antimicrobial activity comparing to Ag^+ ions - Able to interfere with biofilm formation - Provide high dispersion stability for the NPs - Broad-spectrum activity - Au NPs are safer and more colloidal stable than Ag NPs	- Body cream with antibacterial and antifungal agents - Film formation - Non-dripping	(Fratoddi, 2018; Oun et al., 2019)
Anti-aging cream	Nanocellulose	- Nanocelluloses act as immediate anti-wrinkle agents by combining the soft-focus effect due to their morphology, the moisturizing effect due to their high water holding capacity, and the filler effect that reduces the skin roughness.	- Anti-wrinkling effect - Water protection	(Rizzi et al., 2021)

	Nanocellulose decorated with Au and Au nanopartilces as an elucidated anti-aging agent	- Multiple and not fully elucidated anti-aging action (e.g., antioxidant effect and prevention of ECM protein modifications). - Physiologically involved in dermal regeneration - Mainly used in beauty devices	- Anti-wrinkling effect	(Souto et al., 2020)
Cleansing agents	Face mask composed of nanocellulose	- A cleansing product for over accumulated oil on the skin. - Efficient removal of skin soil while preserving barrier integrity	- Cleansing effect	(N. Sharma et al., 2018)
Skin regenerative membranes	Cellulose nanofiber based wound dressing in skin graft donor site treatment	- Wood based cellulose nanofibers wound dressing tested in split-thickness skin graft donor site treatment for nine burn patients in clinical trials	- Cellulose nanofiber dressing seems promising for skin graft donor site treatment - Biocompatible, attaches easily to wound bed, - remain in place until donor site has renewed.	(Hakkarainen et al., 2016)
Sensor platform for wearable Skin Biosensor	Skin-adherent biosensors based on pure nanocellulose fibers substrate	- Sensor platform based on pure nanocellulose fibers substrate - enables the detection of uric acid, 17β-estradiol, Pb^{2+} and Cd^{2+} in sweat. - Screen printing on cellulose based membranes allow optimal skin integration in wearable technologies.	- Biocompatible adherent to human skin used in electrochemical sensors	(Silva et al., 2020b)

Table 3. Patents related to the use of nanocelluloses for skincare and cosmetic products

Nanocellulose type	Publication Date	Patent number	Patent description
Microcrystalline cellulose (MCC)	April 01, 2004	WO2004026263A2	Cosmetic composition containing microcrystalline cellulose
	August 12, 2004	US20040156811A1	Decorative skin and hair cosmetics containing microcrystalline cellulose as an enhancing agent
	August 26, 2004	WO 2004071322	Colloidal microcrystalline cellulose toothpaste of reduced stringiness and improved flavor release
	June 14, 2007	WO2007066222A1	Cellulose gel formulations
	January 18, 2011	US20090130287A1	Microcrystalline cellulose compositions
	December 06, 2011	CA 2488158C	Stable oral compositions comprising microcrystalline cellulose and a surface-active agent
	April, 11, 2013	WO2013052114A1	Stabilizer composition of microcrystalline cellulose and carboxymethylcellulose, a method for making, and uses
Nanocellulose spherical particles (NCSPs)	October 21, 1997	FR2769836B1	Use of essentially amorphous cellulose nanofibrils associated with organic polyhydroxy compounds in cosmetic formulations
	February 02, 2017	WO2017018554	Nanocellulose utilizing non-lignocellulosic biomass, and cosmetic composition and superabsorbent material containing the same
	August 25, 2015	US9114077B2	Nanocrystals for use in topical cosmetic formulations and method of production thereof
	February 2, 2016	CA2956661A1	Method for producing functionalized nanocrystalline cellulose and functionalized nanocrystalline cellulose
	June 7, 2018	CA3044721A1	Sunscreen composition comprising

			nanocrystalline cellulose
	June 7, 2018	CA3044727A1	Cosmetic composition comprising nanocrystalline cellulose, method, and use thereof
	October 11, 2018	WO2018185768A1	Haircare compositions
	October 9, 2019	EP3548144A1	Powdery cosmetic composition comprising nanocrystalline cellulose
	February 13, 2020	WO2020031186	Cellulose-based topical formulations
Cellulose nanofibers (CNFs) and nanocrystals (CNCs)	June 29, 2001	FR2794466B1	Composition in the form of an oil-in-water emulsion containing cellulose fibrils and its particular cosmetic uses
	September 7, 2007	JP2009062332A	Cosmetic composition containing fine fibrous cellulose and/or its composite material
	April 13, 2011	EP 2 307 100 A2	Liquid cleansing compositions comprising microfibrous cellulose suspending polymers
	October 11, 2012	JP2012193139A	Cosmetics having an excellent moisturizing property, less skin irritation and non-stickiness
	June 12, 2018	CN108143680B	Plant cellulose nanofibril antibacterial moisturizing mask and preparation method thereof
	July 3, 2018	US10010490B2	Cosmetic composition comprising cellulose fibers with small fiber diameter and comparatively small aspect ratio
	January 3, 2020	KR20200000579A	Composition for skin care enhancement including denaturalized cellulose
	April 1, 2020	KR102095715B1	Mask pack composition comprising a cellulose nanofiber
	October 22, 2020	US 16/854944	Topical delivery system containing cellulose nanofibers
	November 25, 2020	EP3741354A1	Sunscreen agent comprising cellulose nanofibers
	May 4,	WO2017075402A1	Sweat sensing devices based nanocellulose platform with

	2017		electromagnetically shielded sensors, interconnects, and electronics
	July 20, 2017	WO2017122224A1	Cellulose nanocrystals based composite formulation for wound healing and a process for the preparation thereof
Bacterial nanocellulose (BNC)	November 29, 1998	US4788146A	Liquid-loaded pad for medical applications
	October 11, 2006	EP1473047B1	Microbial cellulose wound dressing sheet, containing polyhexamethylene biguanide, for treating chronic wounds
	October 26, 2006	US20060240084A1	Microbial cellulose materials for use in transdermal drug delivery systems, method of manufacture and use
	August 16, 2007	WO2007091801A1	A sheet device comprising bio-cellulose for alleviating skin damage and relieving skin problem
	December 04, 2007	BRPI0601330A	Topical composition of biocellulose in gel form, spray aerosol, cream and/or aqueous suspension for treatment of epithelial lesions
	February 12, 2009	US20090041815A1	Assembly comprising a substrate comprising biocellulose, and a powdered cosmetic composition to be brought into contact with the substrate
	Mai 05, 2009	FR2924342	Make-up and/or skincare product
	June 05, 2009	FR 2924340A1	Procedure for nail make-up
	December 12, 2009	FR2916971A1	Slimming assembly
	November 30, 2011	EP 2 390 344 A1	Bacterial cellulose film and uses thereof
	January 17, 2012	US20110039744A1	Personal cleansing compositions comprising a bacterial cellulose network and cationic polymer
	May 03, 2012	WO2012057486A2	Cosmetic bio-cellulose mask pack sheet and method for manufacturing the same
	June 27, 2013	WO2013094077A1	Cosmetic bio-cellulose sheet for lips

	February 10, 2015	US8951551B2	Multi-ribbon nanocellulose as a matrix for wound healing
	March 26, 2015	WO2015040106A1	Method for the production of structured cellulose patches or elements and devices made using such a method
	August 6, 2015	US20150216784A1	Cosmetic composition containing fragments of bacterial cellulose film and method for manufacturing thereof
	June 21, 2017	EP3181153A1	Wound care product comprising extracellular matrix-functionalized nanocellulose
	March 12, 2020	KR102088350B1	Cosmetic mask pack sheet of biocellulose and the method for preparing thereof
	April 19, 2001	WO2001026610A1	Electrospun skin masks and uses thereof
	February 2, 2015	US8951551B2	Bacterial nanocellulose as a matrix for wound healing
	November 3, 2016	WO2016174104A1	Modified bacterial nanocellulose and its uses in chip cards and medicine
Cellulose nanoyarns (CNYs)	October 14, 2010	WO2010115426 A1	Skincare compositions for the delivery of Agents
	October 01, 2015	US20150272855A1	Cosmetic sheet formed from nanofibers with controlled dissolution velocity and method of manufacturing the same
	February 04, 2016	WO2016016704A2	Cellulose acetate-based non-woven nanofiber matrix with high absorbency properties for female hygiene products
	November 12, 2019	US 10,470,983	Cosmetic pack and manufacturing method
	November 16, 2019	JP2019001071A	Laminate and sheet for skin adhesion
	July 29, 2020	EP3231320B1	Beauty care pack and method for manufacturing the same

5. Nanocellulose Spherical Particles (NCSP)

Amorphous NCSPs have spherical to elliptical shapes (average aspect ratios of 0.91 to 1.10) with relatively uniform particle sizes (diameter of 50 to 200 nm) (Zhang et al., 2007). The particles are highly amorphous (75 to 80%), which explains their extremely high wettability and water holding capacity together with complete decomposition in the presence of cellulose enzymes. With their small particle size, low aspect ratio along with their strong swelling properties, the NCSPs are not suitable as abrasive peeling or scrubbing media (Bouillon et al., 1998). However, they can be used for advanced skin treatment and healing (Uddin et al., 2019). Some specific features and attributes of NCSPs for utilization in skincare and cosmetic applications are below.

5.1 NCSP as delivery bioactive ingredient

NCSPs can serve as nanocarriers of bioactive ingredients due to their intrinsic properties (fine particle size, high porosity, high abundance of hydroxyl groups, good stability in different solvent systems with no decomposition in the medium) that offer protection of the encapsulated ingredients. The NCSP chemical surface modification by selective oxidation (with nitrogen tetroxide) results in the introduction of carboxylic groups that provide additional hemostatic properties (Barhoum et al., 2019). Active substances for therapeutic skincare (e.g., enzymes) can be adsorbed into the NCSPs and they can chemically bind to the functional groups. Similarly, the sulfate functional groups allow the binding of ions with the enzyme basic functional groups (e.g. histidine, lysine, or arginine). The acidic functional groups (-COO or -SO_3) on NCSPs may bind with antibacterial agents (e.g., Ag or ZnO particles) by irreversible sorption (Tortorella et al., 2020), while other functional groups such as aldehydes also covalently bind to proteolytic enzymes. The encapsulated enzymes are then protected against degradation in the liquid formulation due to protein self-denaturation or autolysis at specific pH ranges and high temperatures (Tortorella et al., 2020). This ensures the long-term stability of the encapsulated enzymes and allows tuning the pH as a function of optimized enzymatic activity. NCSPs can be also used as surfactants and slow-release agents in skincare and cosmetic formulations and wound healing (e.g., creams and lotions) because they improve the application and penetration of cosmetic or drugs into the skin (Tortorella et al., 2020).

5.2 NCSP as a gelling agent

The aqueous dispersion of amorphous NCSPs at moderate concentrations in presence of enzymes (e.g,. trypsin, lysozymes, amidases) leads to a network of cellulosic material forming a gel structure upon cooling of the solution (Abushammala et al., 2010). The formation of a paste with high NCSPs concentrations exhibits good thickening properties and can be used as an additive to prevent phase separation of dispersions (Chirayil et al., 2014).

5.3 NCSP as a moisturizer

The amorphous nature of NCSPs favors the absorption of fluids and provides a higher ability for water uptake compared with CNCs and CNFs, while the surface modification through TEMPO oxidation further enhances the hydrophilicity and superabsorbent properties (Tortorella et al., 2020). Therefore, the NCSPs produced from residual woody or non-woody biomasses (e.g. palm tree leaves, palm trunk, corn stanchion, corn stover, sunflower reeds) has been incorporated in skincare preservatives for moisturizing and alleviating skin wrinkles (patent WO 2017018554),

6. Cellulose Nanofibers (CNFs)

CNFs are thin fibers with a diameter below 100 nm and length in the micrometer range. CNFs can be created using various mechanical procedures, such as high-pressure homogenization, refining, micro-fluidization, ultrasonication, cryo-crushing and grinding (Zhang et al., 2007), in combination with an enzymatic or chemical pretreatment step. Such fibrils contain amorphous and crystalline domains and are characterized by the formation of a dense fibrillary network structure. As the morphology of CNF is similar to that of BNC with higher purity (see later), they have been relatively less exploited for skincare and cosmetics products. However, a cytotoxicity study on CNFs indicated no harmful effect on skin and/or eye irritation when used at appropriate concentrations (Kim et al., 2019). Toxicological effects are explained by the nanocellulose morphology (size, aspect ratio) and physicochemical properties (surface charges) (Lopes et al., 2017). The specific concerns and benefits of CNF for utilization in skincare and cosmetic applications are given in next paragraphs.

6.1 CNFs as formulation modifier

CNFs are generally used as a stabilizer and thickener for liquid systems. It is particularly suited for controlling the viscosity of dispersions and/or emulsions, and thus the applicability and feeling of use. Traditional aqueous thickening and gelling agents for skincare formulations are based on water-soluble natural polymers (e.g. sodium hyaluronate, sodium alginate, xanthan gum), semi-synthetic polymers (e.g. hydroxyethyl cellulose, carboxymethyl cellulose), or synthetic polymers (e.g. carboxy vinyl polymer, polyvinyl alcohol, sodium polyacrylate) (Alves et al., 2020). However, the gelling mechanism for these polymers is based on ionic interactions that are strongly influenced by the pH and significantly alter in the presence of electrolytes. Therefore, sweat can dramatically decrease the viscosity of the applied cosmetic that will consequently slide off the skin. Conversely, CNFs are considered to be a suspending aid or gel-forming agent in the fabrication of cosmetic sheets with better compatibility and salt-resistance (Alves et al., 2020). Moreover, the sensitive feeling of a CNFs-containing gel is enhanced by the reduction of adherence, stickiness and clumping in parallel with a reduced viscosity of the cosmetic formulation during application. The control of the gelling properties with CNFs allows homogeneous drying and formation of a sol after application. The gel formulations with CNFs display thixotropy and can thus be sprayed as a mist without dripping after application. For skincare applications, the mixing of CNFs in an oil-in-water emulsion with at least one fatty phase and one aqueous phase provides good stability to the formulation. During the preparation of formulations with high solid content, the stabilizing effect of the non-soluble 3D fibrillar network of CNFS also prevents the settling and sedimentation of ingredients. Therefore, CNFs is mixed with creams, lotions, pastes, gels, foundations, sera, and ointments (Bacakova et al., 2019).

6.2 CNFs as a functional additive

The high water holding capacity of CNFs (up to 75-100%) is superior to that of other nanocellulose types due to their hydrophilicity and specific morphology with a dense nanofibrillar network. Moreover, the high affinity of CNFs for water can further be increased by surface carboxylation after TEMPO oxidation. The CNFs are therefore preferentially used as a moisturizing component with better performance than traditional polymers, such as collagen or hyaluronic acid (Bacakova et al., 2019). The crystallinity degree of CNFs is an important parameter determining the water absorption capacity and should be between 40 and 50% to make the amorphous cellulose regions accessible for water uptake. Conversely, other nanocellulose types (CNCs and BNC) have a degree of crystallinity above 80% (Sharma et al., 2014).

The dense fiber network also provides improved mechanical reinforcement with high strength, ductility, and excellent elasticity. Due to their high flexibility, the CNFs sheets favorably serve as face masks providing a good fitting and comfortable feeling on the skin and lips (Perugini et al., 2018). Moreover, peeling films can be formed as a separate free-standing layer with a good affinity to the skin (Tang et al., 2021). The formation of a coherent film with CNFs is enhanced by avoiding cracking and the film remains transparent due to the thin fibril diameters. The interaction between fibril bundles has a matting effect on the skin due to the filling of pores and flaws, with an anti-wrinkling and whitening effect. When combined with other polymers such as chitosan, the CNFs can be used to fabricate face masks with antibacterial activity (Ribeiro et al., 2021). The CNFs provide the bulk, whereas the electropositive chitin nanofiber reactive surface amino groups can form strong covalent and hydrogen bonds into a dense cross-linked fiber network with CNFs. The incorporated chitin/chitosan presents intrinsic antimicrobial properties against Gram-negative bacteria, Gram-positive bacteria, and fungi, which can vary in function of the molecular weight and degree of acetylation of chitosan (Ribeiro et al., 2021).

6.3 CNFs as drug delivery

The CNFs are used as topical encapsulating and delivery agents of active skincare products, providing better regulation of the ingredient penetration into the skin through controlled release. The drying of a cellulose network structure in presence of active compounds may involve entrapment (Kupnik et al., 2020) and controlled release (Abushammala et al., 2012), depending on the fiber morphology and concentration. The skin delivery systems with CNFs form a three-dimensional matrix that can be further stabilized in combination with external cross-linkers such as alginate (Morais et al., 2020). The encapsulation of essential oils and microalgae is an interesting alternative to increase the exposure time of an active component during dermic and cosmetic applications. Other products may include, e.g., essential oils, plant extracts, repair enzymes, sunscreen active components, humectants, botanical extracts, peptides, vitamins, antioxidants, or preservatives. Such cosmetic treatments may offer long-term improvement of the skin texture, smoothness, and healing of photochemically damaged and red or sensitive skin (Morais et al., 2020).

7. Cellulose nanocrystals (CNCs)

CNCs are short rod-like fibers with a diameter of 5 to 10 nm and a length below 100 nm. The crystallites are fabricated by chemically removing the amorphous domains using ultrasound treatment and strong acid hydrolysis with a selection of concentrated sulfuric acid, hydrochloric acid, hydrobromic acid, or phosphorous acid depending of the required properties. The dispersibility and rheological features of CNCs vary as a function of the chosen acid (Blanco et al., 2018). Specifically, CNCs obtained by phosphoric or sulfuric acid hydrolysis disperse readily in water because of the abundance of highly polar phosphate or sulfate groups at their surface. Conversely, CNCs fabricated by hydrobromic or hydrochloric acid hydrolysis cannot be easily dispersed as their aqueous suspensions tend to flocculate (Wulandari et al., 2016). Alternative green methods were recently developed using enzymatic-assisted hydrolysis and recyclable ionic liquids to reduce environmental contamination from acidic wastewater (Meyabadi et al., 2014). The structures of CNCs produced from enzymatic-assisted hydrolysis have extremely high crystallinity and better mechanical strength and stiffness than acid hydrolysis CNCs (Wulandari et al., 2016).

CNCs display various features suitable for skincare applications, such as a better penetration in the skin membrane, high adhesion, and better permeation via the gastrointestinal wall. Due to their nanosize dimensions, CNCs can enter and open the individual skin pores for penetration through the lipid layer and epidermis towards the other skin strata (Barhoum, Jeevanandam, et al., 2020). Therefore, CNCs are mainly used for personal care products that are topically applied because they reduce the administered dose, offer a sustained release, and increase customer compliance. Aqueous CNCs suspensions are compatible with skincare products and are added at a typical dilution factor of 50. Inspired by the protective effect of a fiber-rich diet on the intestinal mucosal mechanical barrier, a novel hemp/CNCs-based foundation liquid has been recently formulated (Figure 6), which effectively solves the post-makeup skin cleaning problems (Tang et al., 2021). The basic features provide easy removal of the foundation through simple wiping, which avoids skin damage caused by excessive cleansing. The CNCs foundation liquid has an excellent performance in terms of biological compatibility, water resistance, and controlled skin penetration. Some main functionalities of CNCs for use in cosmetics are discussed below.

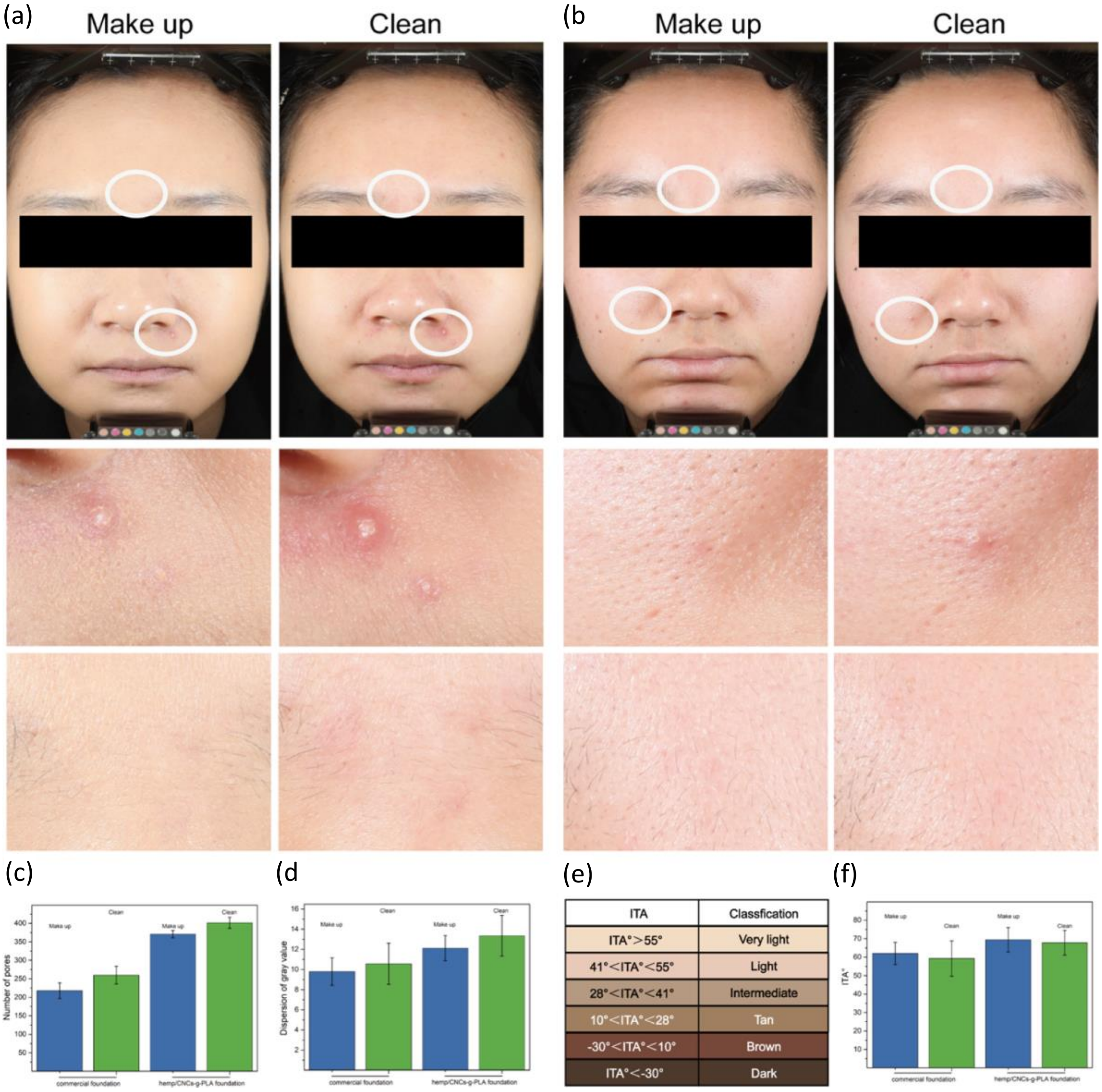


Figure 6. Cellulose nanocrystals (CNCs) for skin barrier protection by preparing a versatile foundation liquid: (a) Images obtained under a standard flashlight after using commercial make-up and wiping off; (b) Images after using foundation liquid based on hemp/CNCs and wiping off; (c) Number of pores on both sides of the nose was counted; (d) Variations in gray value of facial skin was measured; (e) Schematic diagram of the individual typology angle (ITA°) and its colour classification; (f) ITA° values of commercial and hemp/CNCs foundation liquid after making up and wiping off (Tang et al., 2021).

7.1 CNCs as formulation modifier

The CNCs particularly play an important role as stabilizing agents for Pickering emulsions, in which solid particles organize at the liquid/liquid interface to prevent coalescence of the liquid droplets (Figure 3a) (Tang et al., 2019). Oil-in-water and water-in-oil emulsions contain two or more immiscible phases and one is dispersed as droplets in the other. The system is thermodynamically unstable and usually stabilized by surfactants or amphiphilic molecules to prevent phase separation by reducing the interfacial energy (Kralchevsky et al., 2005; De et al., 2015). Alternatively, the stabilization of emulsions with solid particles is governed by the formation of a physical boundary through a particulate network (Chevalier et al., 2013; Wu et al., 2016). Although several particle morphologies can be used, emulsions are more efficiently stabilized with a smaller number of rod-like particles than spherical particles (Kontturi et al., 2018). The CNCs display better-stabilizing features than native cellulose fibers (Costa et al., 2018); however, unmodified CNCs with many surface hydroxyl groups are often too hydrophilic for oil-in-water emulsion stabilization (Lu et al., 2018). The CNCs that are chemically modified with carboxylic groups, succinic anhydride or fatty acids display more balanced hydrophilic/hydrophobic surface properties and consequently higher emulsifying capacity. As such, the surfactant-free emulsions for skin drug delivery system and pharmaceutical uses can be formulated using natural nanomaterials as stabilizing agents (Tang et al., 2018).

7.2 CNCs as functional filler and additives

CNCs represent an alternative to traditional fillers such as graphene, carbonate, silica, calcium, or organic polymer particles (polyphenols) and polysaccharides (chitin, starch) (Fujisawa et al., 2017). Due to their high degree of crystallinity, CNCs are physically and chemically inert and only interact weakly with other active ingredients in the formulation. However, the presence of residual sulphuric acid charges after hydrolysis may interfere with the dispersion stability of other ingredients. Therefore, the sulfuric acid concentration can be reduced through a naturalization procedure by dilution of the CNCs suspension and separation of the hydrolysed cellulose through centrifugation (Barhoum et al., 2019). The increase in pH of the CNCs acid environment towards neutral pH in presence of calcium carbonate or barium carbonate allows the conversion of the sulphuric residues into white inorganic pigment. The *in-situ* formation of this white pigment is a cheap alternative to TiO_2 and ZnO and is less abrasive than pure inorganic nanomaterials (Samyn et al., 2018).

The high crystallinity of CNCs as compared to CNFs, endows them with extremely high mechanical stiffness, strength and hardness. Therefore, CNCs can compete with the intrinsic abrasive properties of inorganic pigments, such as silica carbide, silica dioxide, or aluminum oxide for scrubbing. The CNCs are suited as an additive for gentle skin cleansing, dentifrices or peeling, as they enhance the effects of mechanical scrubbing and removal of dead skin tissue. Inorganic materials are harder than CNCs, but they may be too abrasive and cause skin damage. Conversely, CNCs have better-balanced properties for abrasive cleaning as their nanoscale size does not hurt the skin and provides a gentle feeling without scratching (Panchal et al., 2019). Other nanocellulose types with higher amorphous content are less efficient as peeling additives as they are too soft and become even softer after swelling in a water environment. CNCs can also improve the appearance of photo-aged skin and stimulate wound healing by reducing scar formation (Singh et al., 2016).

7.3 CNCs as hair-straightening agent

In combination with good film-forming properties, CNCs may provide a functional protective layer onto hair, thus enhancing and restoring the straightening effect of the hair. The negatively charged CNC surfaces with sulfate groups provide the binding to cationic compounds and/or hair (Kontturi et al., 2018). This demonstrates that cationic surfactants can facilitate the CNC binding to the hair through electrostatic interactions (coulomb forces) and/or additional hydrophobic interactions. Indeed, the hair surface is naturally hydrophobic in presence of lipids. Moreover, CNCs contribute to the reconfiguration of keratin structure in hair, offering mechanical support to the fresh keratin structure upon straightening and/or shielding from ambient humidity and pollution (Soodeh et al., 2020).

7.4 CNCs as nanocarrier for UV-blockers

The optical properties of CNCs suspensions are suitable for utilization as nanocarriers for UV-blockers and protection of other cosmetics ingredients from photodegradation (Panchal & Mekonnen, 2019). The CNCs suspensions have a maximum UV absorbance peak at around 278 nm, and their absorption intensity is influenced by the acid hydrolysis duration (Bongao et al., 2020). The UV-blocking performance of CNCs is compatible with conventional UV-blockers (TiO_2 or ZnO nanoparticles) that display an absorption peak at 356 to 428 m (Awan et al., 2018). Therefore, CNCs might be a potential alternative to mineral-based nanoparticles in cosmetics with UV protection features, remediating facial aging by sun exposure. The CNCs regulate interaction with light through absorption, scattering, transmission and reflection, and they can highlight the natural appearance with matt or soft-focus effects of the skin while hiding imperfections. The refractive index of particles for a soft-focus should differ from the value of the medium in which the particles are present, but it cannot be too high as it would give an unnatural look to the skin with high opacity. The *in-situ* growth of UV-blockers such as ZnO nanoparticles onto the CNC surface (melamine formaldehyde-covered CNCs) was tested for smart skincare applications (Awan et al., 2018). The CNCs/ZnO hybrid nanomaterials present attractive photocatalytic activity and UV absorption under solar radiation, providing an intelligent skincare formulation with high photocatalytic efficiency. The use of CNCs offers various benefits, such as, e.g., a better-controlled growth and dispersion of ZnO in the medium, a higher specific ZnO surface area, and preventing the recombination of active photocatalytic sites.

7.5 CNCs as nanocarrier for bioactive ingredients

CNCs have been tested as nanocarriers of topical or bioactive substances for transdermal delivery and advanced skincare products including therapeutic lotions, liposomal dispersions and creams. In relation with their size and high specific surface area, CNCs are reactive for binding to substances and allow better transdermal penetration and delivery through the skin. The CNCs reactivity facilitates the chemical binding of active health components, such as, e.g., *(i)* proteolytic enzymes and amino acids that provide gentle skincare in combination with peeling, and *(ii)* lipases for selective skin degreasing (Chirayil et al., 2014). CNCs have also been used as a carrier for the topical delivery of hydroquinone to improve its therapeutic efficacy and decrease the cosmetic skin effects (Sunasee et al., 2016). Hyperpigmentation is a frequent skin disorder where hydroquinone limits melanin production and skin discoloration. The preparation of hydroquinone-CNCs complexes was done by simply incubating hydroquinone with CNCs suspensions. CNCs containing rutin (flavonoid) as an active ingredient are used for toothpaste applications to replace hydroxyapatite, the main component of tooth enamel (Hameed et al., 2019). For lipsticks, colored ingredients (dye molecules) are typically in contact with the skin, whereas the lipstick made with dyed-CNCs (CNCs-lipstick) would reduce the contact. The use of dyed-CNCs declines the rate of dye molecules diffusion so the migration of color from the lipstick is reduced and complete removal of the color after application can be achieved (Figure 7) (Kang et al., 2019). In addition, CNCs with anti-oxidant properties provide protection as a scavenger of free radicals and prevent skin degradation (Kang et al., 2019).

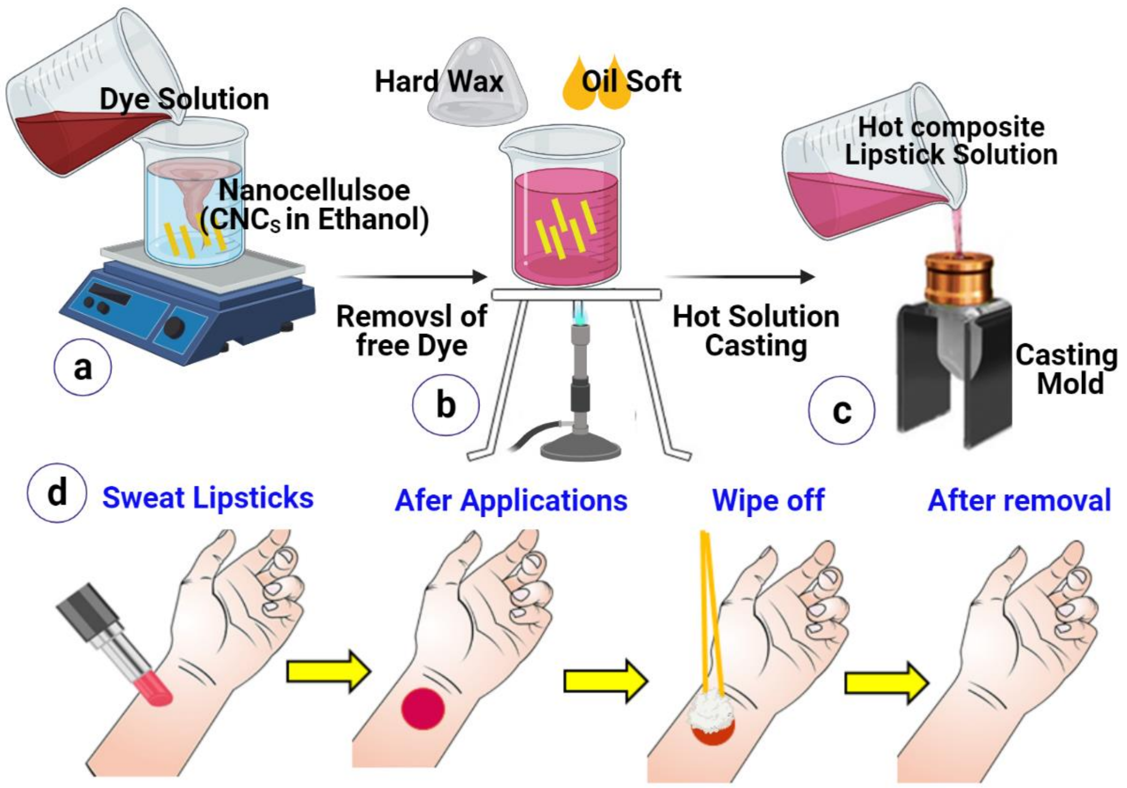


Figure 7. Schematic presentation showing the use of CNCs as dye carriers and protective materials in a lipstick matrix for inhibiting color migration: (a) loading of the dye and removal of excess dye; (b) preparation of the lipstick from oil, wax, solvent and dye-CNCs; (c) casting of the prepared solution; (d) application and removal of lipstick with reduced diffusion rate of dye molecules. Figure adapted from the abstract of (Kang et al., 2019) using Biorender.

8. Bacterial nanocellulose (BNC)

BNC forms a dense network of cellulose fibrils produced by aerobic micro-organisms such as Gram-negative bacteria, e.g. *Gluconacetobacter xylinus* (formerly known as *Acetobacter xylinum*). Unlike native cellulose fibers that are scaled down to nanoscale units, BNC is directly produced as nanoscale fibril units in the culture medium through fermentation (Jacek et al., 2019), and complex biochemical conversion (Meftahi et al., 2018). Its production mainly involves the assimilation of carbon sources (i.e. polymerization of fructose, mannitol, sorbitol, glucose, cellobiose, glycerol, galactose, lactose, sucrose, maltose, monomers) and secretion of cellulose in weak acidic conditions (pH 4.5 to 6.5). During fermentation, micro-organisms travel freely in the medium or are connected to cellulose fibers and produce a swollen gel structure. After synthesis, dead micro-organisms and cell waste is removed during purification by repeated alkaline washing in a hot sodium hydroxide solution or a strong oxidizing agent until neutral pH is reached (Abouelkheir et al., 2020). More recently, this cleaning step with aggressive chemicals could be replaced by autoclave and gamma irradiation treatment. Although the culture techniques are complex, the lower energy that is required for production and purification makes BNC a more environmentally friendly material. The quality of the synthesized ribbon-like BNC fibers highly depends on the washing efficiency (Abouelkheir et al., 2020).

BNC is characterized by a left-hand twist and long aspect ratio, with very high crystallinity (up to 86%), ultra-high purity (absence of non-cellulosic substances), and consequently superior mechanical properties compared with CNFs from plant sources (de Amorim et al., 2020). The incorporation of functional additives or cellulose derivatives in the bacterial culture medium together with dextrose during BNC secretion allows to the production of *in-situ* functionalized nanofibers. The development of a nanofibrillar network is controlled by the motion of the bacteria during synthesis (Pacheco et al., 2018), and provides ideal porosity to be used as medical membranes with excellent mechanical features, purity, malleability, biodegradability, tensile strength, porosity, and easy handling (Meftahi et al., 2018; Ullah et al., 2016). In cosmetics, BNC is mainly used in facial scrubs, facial masks, personal cleansing formulations, and contact lenses (Ullah et al., 2016). The extensive use of BNC as wound dressing materials is outside the scope of this review as it has been widely discussed in other reviews (Bielecki et al., 2012).

8.1 BNC as formulation modifier or additive

The BNC can be added in skincare and cosmetic formulations as a rheological modifier or stabilizing agent for oil-in-water emulsions. In parallel with previous descriptions of CNFs, the emulsions with BNC do not require additional surfactants that may be harmful or induce skin irritation (Paximada et al., 2016). The BNC permits reducing the percentage of surfactants used in a liquid matrix without changing its rheological features (Paximada et al., 2016). The BNC is compatible and provides stabilization with other ingredients present in a scrub, such as olive oil, aloe vera extract, ascorbic acid, vitamin C, or powdered glutinous rice. The inclusion and topical delivery of drugs in cosmeceuticals and medical skincare (wound healing and burn repair) including BNC can be also tuned for a controlled stimulus-responsive release.

The rheological properties of BCN are essential for the application in the facial scrubs, providing homogeneous spread and optimized drying time. The decrease in viscosity as a function of shear rate (i.e., shear-thinning) of BNC is enhanced through conformational changes and alignment of the BNC fibrils under shear. Therefore, an enhanced scrubbing effect is obtained with formulations that include BNC (Hasan et al., 2012). Facial scrubs with BNC have a relatively higher viscosity than commercial scrubs at low shear rates, but viscosities under higher shear are comparable.

8.2 BNC as membranes and facial masks

Facial masks are predominantly proposed for skin restitution, sebum control, deep and fast hydration, and moisturizing. The BNC membranes attracted the most interest as natural skincare facial masks because of their low toxicity, biodegradability, optimized mechanical properties versus porosity, together with skin moistening and hydrating potential (Kolesovs & Semjonovs, 2020). The BNC is a preferred substrate facial mask due to its nanoporous membrane shape with high mechanical stability. In contrast, conventional hydrogel masks are often difficult to handle because they lack high mechanical strength. Also, the CNFs from plant sources have weaker mechanical strength in wet conditions than BNC. The comfort of BNC masks and their satisfactory feeling is mainly related to the high moisture level, water retention (water content up to 98%), and good adherence to the skin (Pacheco et al., 2018). A single application of the BNC highly improves moisture uptake by the skin (Mohite & Patil, 2014). After mask removal, improvements in skin moisture, sebum, elasticity, texture, dullness, and desquamation levels were reported (Press, 2011). As a result, the skin hydration performance of BNC mask is 7 to 28% higher than common creams. The BNC masks additionally help to reduce the sebum concentrations and saturation, resulting in a brightening effect, smooth feeling, translucence and firm look.

Protocols were developed to monitor the BNC mask quality and stability. The changes in water content and nutrient additives at different locations of the mask have been investigated by NIR spectroscopy. A study on the organoleptic properties, viscosity and pH stability of BNC masks from different manufacturers estimated their stability and shelf life at 6 months (Perugini et al., 2018).

9. Electrospun Cellulose Nanoyarns (CNY)

Different systems for electrospinning cellulose derivatives (e.g. cellulose acetate, hydroxypropyl cellulose, hydroxypropyl methylcellulose, ethyl-cyanoethyl cellulose) with suitable solvents are available to produce a regular non-woven fiber mat with nanoscale fibers (Taylor et al., 2008). The properties and morphology of CNYs depend on their processing parameters, such as spinning conditions, solvent system, degree of cellulose polymerization, and final coagulation in a water bath. The CNYs are mostly amorphous, however, the degree of crystallinity of fibers can be controlled by modulating various process conditions, including spinning temperature, flow rate, and nozzle-collector distance (Kim et al., 2006; Miguel et al., 2018).

Although electrospinning is easy to use at a low cost, there is a large number of processing parameters that highly influences fiber generation and nanostructures (Gugulothu et al., 2018). Increasing solution conductivity increases the stretching of the solution jet resulting in CNYs with smaller diameters (Barhoum et al., 2019). Solvent volatility must be in a certain range as the more volatile solvents result in ribbon/flat fibers and fibers with surface pores. The higher viscosity of the cellulose solution will induce a larger CNY diameter, while the higher temperatures will result in lower viscosity and thinner CNY diameter (Bubakir et al., 2019).

9.1 CNY as membranes and masks

The CNY membranes are frequently used in skincare formulation as wound dressings, skin covers, protective sheets, healing agents, or masks (Fathilah et al., 2019). The electrospun mat can directly be applied onto the skin without the need for an intermediate fabrication step, for instance using a transient, charged receiver to first collect the fibers into a mat before application on the skin. The mask may function as a hydration medium or as a medium to absorb excess moisture or oil from the skin. The superabsorbent capacities due to the large pore volume, surface area, and porosity, together with high mechanical strength of the porous membranes can be adapted by modulating the concentration of a spinning solution from cellulose acetate in N, N-dimethylacetamide (Yadav et al., 2016). Recently, the functionalized CNY membranes were fabricated by blending silver sulfadiazine within the cellulose acetate spinning solution, resulting in wound dressing membranes with embedded antibacterial properties (Khan et al., 2019).

9.2 CNY as a topical delivery medium

The bioactive agents or nutrients (e.g. peptides, vitamins) can be incorporated into electrospun CNY single fibers or membranes to enhance skin healing and cleansing, or to provide specific functions for a medical purpose (e.g., whitening, anti-wrinkle, moisturizing, skin irritation relief, skin elasticity enhancement, antibacterial activity). An advantage of CNYs is that skincare ingredients can be directly incorporated in liquid form (as a solution or dispersion) in the mixture used to electrospun the fibers. Because of their high surface area and small interstices, the penetration of active ingredients into the skin is enhanced with a strong increase in drug efficacy (Nafisi et al., 2017). The CNYs of hydroxypropyl cellulose and polyurethane have been used for transdermal drug delivery, with reduced skin irritation and diffusion-controlled release of the encapsulated drug (Gencturk et al., 2016). However, when cellulose acetate is combined with cream of rubber extracts, fewer influences on the efficiency and/or degradation of the incorporated bio-active components were noticed when used as facial masks (Suwannateep et al., 2015).

The adhesion of electrospun CNY membranes to the skin is critical and can be resolved by the fabrication of a double layer and/or the addition of proper additives. The polymer fibers incorporated in the mat can vary and/or can be combined by co-electrospinning in a laminated mat to tune the density, mechanical strength, chemical composition and physical properties in order to provide intimate skin contact and absorption. Therefore, the electrospun CNY is sometimes used as outer layer in a multilayer dressing in combination with a second layer of polymer nanofibers that contain the active cosmetic component for migration into the skin. The additional layer also mechanically supports the shape of a weak and moisturized cellulose layer in beauty care packs. In particular, the release and easy peeling after use can be adapted and/or the masks made from water-soluble cellulose derivates can be easily washed from the skin with water.

10. Emerging nanocelluloses applications in wearable skin sensors and skin regeneration

Use of nanocelluloses in skin regeneration, wound healing, and wearable skin sensors have attracted widespread attention over the past decades. Interestingly, nanocelluloses have been applied to daily life in health monitoring sectors, motion monitoring, human-computer interaction, and artificial intelligence (Herrmann et al., 2021; Z. Wang et al., 2021; Zhao et al., 2021). Nanocellulose as skin biocompatible materials have also shown a vital role in the development of wearable skin sensors, for in-situ mentoring of biomarker diseases release from the skin (Figure 8a). In relation to skin biosensors, nanocellulose membranes have been successfully investigated as sensing platform for bioreceptors (e.g. enzymes, antibodies, aptamers) immobilization, due to its high surface area, characteristic particle size, and pore structure. Surface functionalization (-OH, -COOH, -SO_3H) of nanocelluloses allows to accommodate binding sites for bioreceptors, and then selective binding with the targeted biomarkers released from the skin. Nanocelluloses effectively address the skin sensors problems not only to fabricate flexible and skin biocompatible wearable sensors, but also lightweight property, cost-effectiveness, disposability, and robustness (L. Dai et al., 2020), (H. Xu et al., 2020). Recently, nanocellulose hydrogels can also be used as a reducing and stabilizing agent, which provides plasmonic NPs (Ag and Au NPs) with strong stabilization and allows them to monodisperse in solutions without aggregation (Divya et al., 2021). BNC have been used as sensor platforms to host optically active species to detect E. coli (Cheeveewattanagul et al., 2017). Recently, Silva et al. developed wearable sensing platforms made of screen-printed carbon electrodes on the bacterial cellulose-based platform. This sensor can detect 17β-estradiol, uric acid and toxic metals (Pb^{2+}, Cd^{2+}) in sweat with limits of detection of 0.58, 1.8, 0.43 and 1.01 μM, respectively (Silva et al., 2020a). In another study, Xu et al. developed a flexible piezoresistive electronic skin (E-skin) by TEMPO-oxidized CNFs and sulfonated-CNTs. The flexible sensor exhibited an extremely high sensitivity of about 4.4 kPa^{-1}, ultrafast response time below 10 ms, ultralow detection limit of 0.5 Pa, good stability (>11000 cycles) and mechanical strength of up to 184 MPa (H. Xu et al., 2020).

Nanocellulose with an exceptional skin-substitute natural polymer routinely used for wound dressing and offers unprecedented potential as a scaffolds for wound healing. In contract to nanocellulose produced from plant sources, BNC may have more advantageous for application of the skin as they are highly biocompatible with human tissues (J et al., 2020). BNC morphology and high purity mimics the nanoscale architecture of the native extracellular matrix, they have been investigated as temporary substrate for the adhesion and growth of skin cells for extensive burns and skin damaged by mechanical traumas or chronic ulcers (J et al., 2020). Dried BNC membranes display high permeability for liquids and gases and low skin irritation alongside adhesive-free adherence to skin moisture (Fontana et al., 1990; Portela et al., 2019). Nanocelluloses have been used in reconstructing the structural and functional components of skin, reducing scar formation, and improving the quality of wound healing. Every year, millions (Chung et al., 2020) of patients are waiting organ donors and suffer from long transplant waiting lists. For cell attachment and proliferation, the scaffolds must be coated with bioactive substances, or surface modification, or encapsulate cells in hydrogels to allow the self-assembly of cell aggregation and 3D print cells directly in the form of a scaffold (Figure 8b). An ideal biocompatible scaffold has to possess a surface that is suitable for cell attachment and 3D interconnected porous structures for extracellular matrix formation and vascularization. Nanocellulose provides biocompatible and mechanical properties, and cell adhesion for cellular attachment.

Nanocellulose hydrogels are characterized by a nanofiber network structure that confers mechanical stability and flexibility and high biocompatibility with skin tissue (Figure 8c). Nanocellulose hydrogels has a water content of up to 95% and this creates a moist environment and prevents excessive fluid loss through the wound healing process.

Nanocellulose hydrogels can significantly reduce intradermal temperature and have a cooling effect, which is based on evaporation. Electrospinning and 3D printing of nanocelluloses (hydrogels) allows fabricating scaffolds with more controlled and precise structures compared to salt-leaching, freeze-drying, and foaming techniques (Chung et al., 2020). Compared with synthetics polymers, nanocelluloses also stand out in the field of 3D printing (bioinks formulation) serving as platform biomaterial owing to their high mechanical strength as well as the structural similarity mimicking natural extracellular matrix. However, the big challenge is to develop printable formulations and to keep the printed scaffolds stable. Recent cell tests have shown that the 3D-printed of cross-linked nanocellulose hydrogel scaffolds supported fibroblast cells' proliferation, which was improving with increasing rigidity. These 3D-printed scaffolds render nanocellulose a new member of the family of promising support structures for crucial cellular processes during wound healing, regeneration, and tissue repair (C. Xu et al., 2018).

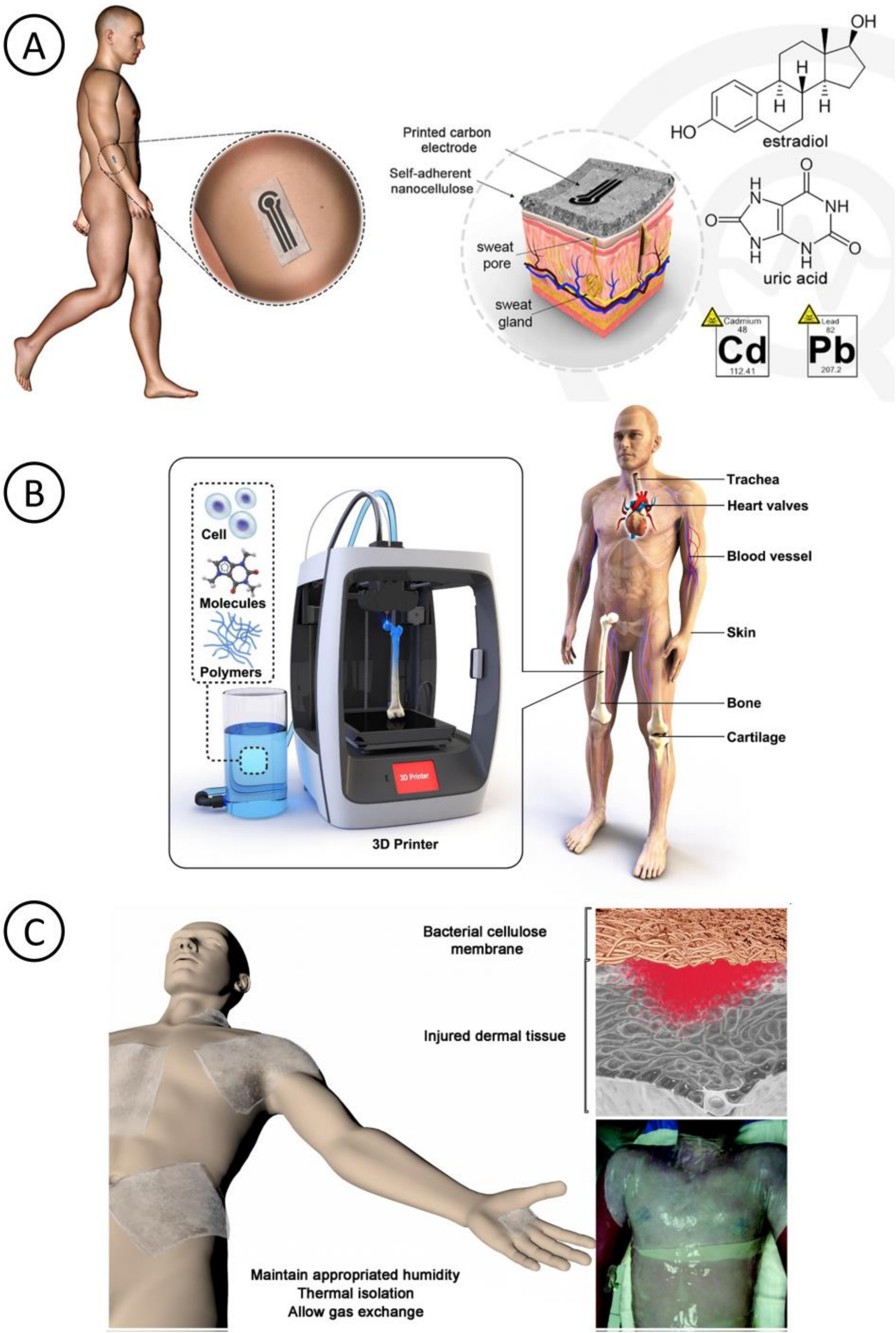


Figure 8. Emerging applications of nanocelluloses in healthcare: (a) Screen-printed carbon electrode deposited on a bacterial nanocellulose substrate for non-invasive detection of biomolecules in biological fluids released from the skin (Silva et al., 2020a). Copyright Elsevier. (b) 3D printing of nanocellulose hydrogel with cells and bioactive molecules for skin tissues and organs repair (Chung et al., 2020). Copyright Frontiers, (c) use of bacterial

cellulose membrane as skin regenerative materials for skin burns and wound healing. Copyright Elsevier (de Oliveira Barud et al., 2016).

11. Safety and regulatory aspects of nanocelluloses in cosmetics

Skin biocompatible products are in contact with the human body after application by pouring, sprinkling, rubbing, or spraying. As skincare products are often accompanied by drugs, bioactive components, or coloring materials also have additional therapeutic effects, a regulatory framework for labeling and usage is needed. As demonstrated in this review, nanotechnology has high potential in the skincare industry due to easy penetration through the skin towards the targeted tissue. In parallel, the World Health Organization (WHO) expressed concerns about the effect of nanomaterials on human health and administrative directives have been introduced (Pastrana et al., 2018). However, the regulation of cosmetics remarkably vary in US, Canada, Europe and Japan (Bilal et al., 2020).

According to the Food and Drug Administration (FDA), the physicochemical characteristics, agglomeration and size distribution of nanomaterials are some of the key points in their assessment, depending on the properties such as morphology, solubility, density, porosity, stability and impurities (Tan et al., 2018). Therefore, FDA published separate information on the health and safety guidance for the use of nanomaterials and nanotechnological approaches in skincare formulations and identified potential safety risks and their evaluation criteria (Bilal et al. 2020). Pre-market approval by FDA is essential for skincare products and drugs (both finished products and ingredients), and the manufacturer must ensure their safety before entering the marketing (Katz, 2007, Fytianos et al., 2020). It emphasizes that skin biocompatible products and their constituents must not be misbranded or adulterated (Effiong et al., 2020).

According to the European Commission (EC), the safety of nanomaterials in skincare and cosmetic products should focus on their intrinsic physicochemical characteristics and additional toxicological data. The EC Regulation (2007) provides a list including all skincare products and their ingredients, type, quantity, manufacturing, marketing, and the manufacturer's responsibilities. In Europe, all ingredients and nanomaterials used in skincare products must undergo a safety assessment and be notified six months before the marketing (Jeevanandam et al., 2018). Moreover, animal testing is strictly prohibited for the collection of toxicological information and hazard determination. Therefore, safety assessment of nanomaterials and nanocarriers is based on *ex-vivo* and *in-vivo* immunotoxicity tests (Bernauer et al., 2019).

The toxicological tests for various types of nanocelluloses with different physicochemical features, such as rigidity or surface properties, evoke variable results (Roman, 2015). The main parameters and physicochemical properties of nanocelluloses that affect toxicological studies and main outcomes are summarized in Figure 9 (Ventura et al., 2020). Nanocelluloses in powder or gel form may cause immunological reactions related to their agglomeration propensity when dispensed *in-vivo* or *in-vitro* (Ventura et al., 2020). The bioavailability, cellular uptake and interaction with sub-cellular constituents is largely influenced by the agglomeration of the nanocellulose. Therefore, the nanocellulose uptake and the interaction of its functional groups with the cell membrane – and hence downstream biological responses – will either be enhanced or retarded by surface functionalization depending on their surface charge, hydrophobicity and surface chemistry (Ventura et al., 2020).

In general, the nanocellulose absorption into cells is low and there was observed no direct induction of oxidative stress or no significant genotoxic and cytotoxic impact (Ventura et al., 2020). Nevertheless, macrophages caused moderate to severe inflammatory reactions owing to their phagocytic function mostly for NCSPs and CNCs. In comparison, CNFs and BNC were not phagocytized but represented notable genotoxicity for both *in-vitro* (chromosomal destruction) and *in-vivo* (DNA destruction) testing. To date, various studies revealed adverse effects such as interstitial fibrosis, pulmonary inflammation, bronchioloalveolar hyperplasia, granuloma and even cancer (Ventura et al., 2020). In comparison, the *in-vitro* effects such as cytotoxicity, genotoxicity and immunotoxicoty evidenced for nanocelluloses were inferior to those of other nanomaterials (e.g., carbon nanotubes). Considering the various physicochemical properties of nanocelluloses, however, the design of safe nanomaterials is essential for sustainable innovative applications in order to impede adverse health effects by oral, dermal or respiratory human exposure (Ventura et al., 2020).

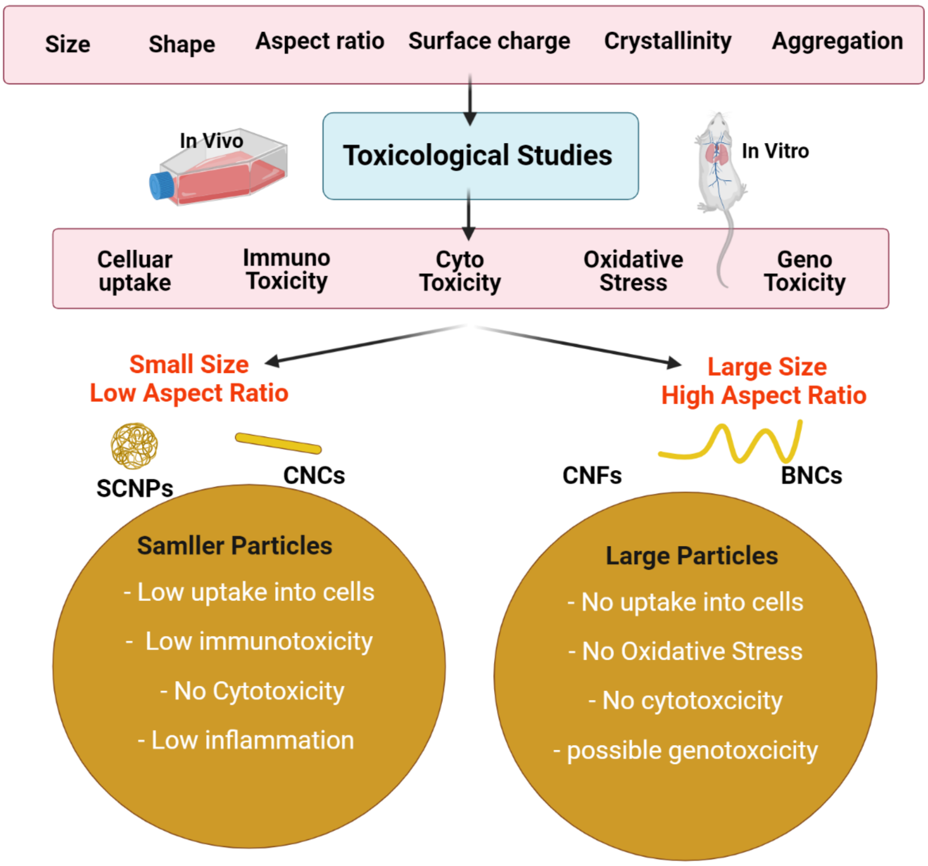


Figure 9. Schematic representation of the main physicochemical properties of nanocelluloses affecting toxicological studies and their main outcomes.

12. Limitations and challenge of nanocelluloses in skincare formulation

Nanocellulose has been commercialized for applications in the field of skincare, cosmetics, wound healing, and wearable skin biosensors. At present, it is particularly used as a functional additive in face masks and cosmetics. However, certain drawbacks currently hinder the further expansion of nanocellulose utilization, which are mainly related to its processing conditions:

1) High dispersion stability of nanocelluloses makes their separation from industrial wastewater system difficult and necessitates pH alterations or additions of salt to recover them after water treatment processes (Trache et al., 2020).
2) Due to high polarity and hydrophilic nature of nanocelluloses, the dispersion of nanocellulose in combination with hydrophobic polymers remains a critical issue. However, surface grafting of nanocelluloses with low molecular weight polymers can solve this problem and control the interaction with other skincare ingredients (Buffiere, 2020).
3) Production of nanocellulose from plant sources generally involves acid hydrolysis, alkali treatment, enzymatic hydrolysis, chemical modification. The high water and energy consumption together with limited yield are the main challenges in the preparation process, along with by-product toxicity (Espíndola et al., 2021; Trache et al., 2020).
4) Nanoscale dimension and morphology of nanocelluloses cause some considerations on their potential to affect the environment, humans and nature. The preparation methods, finishing treatments, the degree of aggregation, and chemical modification of nanocelluloses all have significant effects on toxicity (Roman, 2015).

5) Fundamental properties such as rheological behavior, thermal stability, viscoelastic properties and surface functionality impact the industrial application of nanocelluloses and require thorough characterization of the material quality (Li et al., 2015).

6) Standards, test methods and related tools for nanocelluloses are currently being developed and need fast implementation to enhance industrial applications and increase the market introduction of nanocellulose into skincare and healthcare products (Pyrgiotakis et al., 2018).

7) Application of nanocelluloses in skincare, cosmetic, skin tissue regeneration, and wearable skin sensors applications still has many open research questions. Some nanocelluloses (NCSPs and CNCs) have shown oxidative stress in cells and the dosage and concentration of these materials are relevant for human health.

13. Conclusion and outlook

Nowadays, the application of nanocelluloses developing skin biocompatible materials is one of the hottest topics in healthcare and biomedical applications and forms a fast growing economic sector worldwide. Among different types of nanomaterials, nanocelluloses are rapidly emerging for use in personal care, cosmetics, skin tissue regeneration, and wearable skin sensors, owing to their biocompatibility, high aspect ratio, high surface area, abundant surface charge, water holding capacity, biodegradability and mechanical strength. Different nanocellulose types have been recently integrated into a number of cosmetics and personal skin care formulations (e.g. creams, lotions, gels, face masks, make-up powders, hygienic powders, hair care) as well as hydrogels and membranes for wound healing, skin burns, and wearable skin sensors. The nanocelluloses are used in as anti-wrinkle agents, carriers for UV-blocking products, drug delivery systems, compatibilizers, moisturizers and thickeners, with aim of application onto the skin. The nanocelluloses are promising biomaterials for producing green and ecofriendly cosmetics and skincare formulations with higher performance and additional features compared to traditional polymeric materials. However, the specific features of nanocelluloses with different morphologies and resulting physicochemical properties need to be fully understood in order to exploit their full potential. While initially the bacterial nanocellulose was a preferred material for biomedical applications, statistics also show a growth of nanocelluloses produced from wood for skincare applications. In particular, the control of surface functionalities and introduction of nanocomposite particles with multifunctional properties offer high potential for the creation of unique formulations. However, the main challenges facing the spread use of this wonderful nanomaterial in cosmetics and skin care applications are: *(i)* minimizing the cost of production; *(ii)* developing new techniques for large-scale production of nanocelluloses with minimum energy consumption and contamination of the water system; and *(iii)* determination of the efficient dosage, size/aspect ratio, and concentration of nanocelluloses in the formulations applied onto the skin without affecting human health.

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References

Abouelkheir, S. S., Kamara, M. S., Atia, S. M., Amer, S. A., Youssef, M. I., Abdelkawy, R. S., Khattab, S. N., & Sabry, S. A. (2020). Novel research on nanocellulose production by a marine Bacillus velezensis strain SMR : a comparative study. *Scientific Reports*, 1–14. https://doi.org/10.1038/s41598-020-70857-7

Abushammala, H, Hashaikeh, R., & Cooney, C. (2012). Microcrystalline cellulose powder tableting via networked cellulose-based gel material. *Powder Technology*, *217*, 16–20. https://doi.org/10.1016/j.powtec.2011.10.002

Abushammala, Hatem, & Hashaikeh, R. (2010). *Cellulosic gel material as a pharmaceutical excipient* (Patent No. WO/2013/033815).

Aguilar-Toalá, J. E., Hernández-Mendoza, A., González-Córdova, A. F., Vallejo-Cordoba, B., & Liceaga, A. M. (2019). Potential role of natural bioactive peptides for development of cosmeceutical skin products. *Peptides*, *122*(July), 170170. https://doi.org/10.1016/j.peptides.2019.170170

Almeida, T., Silvestre, A. J. D., Vilela, C., & Freire, C. S. R. (2021). Bacterial nanocellulose toward green cosmetics: Recent progresses and challenges. *International Journal of Molecular Sciences*, *22*(6), 1–25. https://doi.org/10.3390/ijms22062836

Alves, T. F. R., Morsink, M., Batain, F., Chaud, M. V, Almeida, T., Fernandes, D. A., da Silva, C. F., Souto, E. B., & Severino, P. (2020). Applications of natural, semi-synthetic, and synthetic polymers in cosmetic formulations. *Cosmetics*, *7*(4), 75.

Awan, F., Islam, M. S., Ma, Y., Yang, C., Shi, Z., Berry, R. M., & Tam, K. C. (2018). Cellulose Nanocrystal-ZnO Nanohybrids for Controlling Photocatalytic Activity and UV Protection in Cosmetic Formulation. *ACS Omega*, *3*(10), 12403–12411. https://doi.org/10.1021/acsomega.8b01881

Bacakova, L., Pajorova, J., Bacakova, M., Skogberg, A., Kallio, P., Kolarova, K., & Svorcik, V. (2019). Versatile application of nanocellulose: From industry to skin tissue engineering and wound healing. *Nanomaterials*, *9*(2). https://doi.org/10.3390/nano9020164

Banerjee, P. K. (1988). Skin cosmetics. *Indian Journal of Dermatology*, *33*(1), 9–12. https://doi.org/10.1002/14356007.a24_219

Barhoum, A., jeevanandam, jaison, Rastogi, A., samyn, pieter, Boluk, Y., Dufresne, A., Danquah, M. K., & Bechelany, M. (2020). Plant Celluloses, Hemicelluloses, Lignins, and Volatile Oils for the Synthesis of Nanoparticles and Nanostructured Materials. *Nanoscale*. https://doi.org/10.1039/d0nr04795c

Barhoum, A., Jeevanandam, J., Rastogi, A., Samyn, P., Boluk, Y., Dufresne, A., Danquah, M. K., & Bechelany, M. (2020). Plant celluloses, hemicelluloses, lignins, and volatile oils for the synthesis of nanoparticles and nanostructured materials. *Nanoscale*, *12*(45), 22845–22890. https://doi.org/10.1039/D0NR04795C

Barhoum, A., Li, H., Chen, M., Cheng, L., Yang, W., & Dufresne, A. (2019). Emerging Applications of Cellulose Nanofibers. In *Handbook of Nanofibers* (pp. 1131–1156). Springer International Publishing. https://doi.org/10.1007/978-3-319-53655-2_53

Barhoum, A., Pal, K., Rahier, H., Uludag, H., Kim, I. S., & Bechelany, M. (2019). Nanofibers as new-generation materials: From spinning and nano-spinning fabrication techniques to emerging applications. *Applied Materials Today*, *17*, 1–35. https://doi.org/10.1016/j.apmt.2019.06.015

Barhoum, A., Samyn, P., Öhlund, T., & Dufresne, A. (2017). Review of recent research on flexible multifunctional nanopapers. *Nanoscale*, *9*(40), 15181–15205. https://doi.org/10.1039/c7nr04656a

Bernauer, U., Bodin, L., Chaudhry, Q., Coenraads, P. J., Dusinska, M., Gaffet, E., Panteri, E., Rogiers, V., Rousselle, C., Stepnik, M., Chaudry, Q., Coenraads, P. J., Dusinska, M., Ezendam, J., Gaffet, E., & van Wijnhoven, S. (2019). Guidance on the safety assessment of nanomaterials in cosmetics. *Luxembourg: European Commission: Scientific Committee on Consumer Safety*, *2019*. https://doi.org/10.2875/40446

Bielecki, S., Kalinowska, H., Krystynowicz, A., Kubiak, K., Kołodziejczyk, M., & De Groeve, M. (2012). Wound dressings and cosmetic materials from bacterial nanocellulose. *Bacterial Nanocellulose: A Sophisticated Multifunctional Material*, *9*, 157–174.

Bilal, M., & Iqbal, H. M. N. (2020). New Insights on Unique Features and Role of Nanostructured Materials in Cosmetics. *Cosmetics*, *7*(2), 24. https://doi.org/10.3390/cosmetics7020024

Blanco, A., Monte, M. C., Campano, C., Balea, A., Merayo, N., & Negro, C. (2018). Nanocellulose for industrial use: Cellulose nanofibers (CNF), cellulose nanocrystals (CNC), and bacterial cellulose (BC). In *Handbook of Nanomaterials for Industrial Applications*. Elsevier Inc. https://doi.org/10.1016/B978-0-12-813351-4.00005-5

Boisset, C., Fraschini, C., Schülein, M., Henrissat, B., & Chanzy, H. (2000). Imaging the enzymatic digestion of bacterial cellulose ribbons reveals the endo character of the cellobiohydrolase Cel6A from Humicola insolens and its mode of synergy with cellobiohydrolase Cel7A. *Applied and Environmental Microbiology*, *66*(4), 1444–1452. https://doi.org/10.1128/AEM.66.4.1444-1452.2000

Bongao, H. C., Gabatino, R. R. A., Arias, C. F. H., Jr, E. R. M., & Magdaluyo Jr, E. R. (2020). Micro/nanocellulose from waste Pili (Canarium ovatum) pulp as a potential anti-ageing ingredient for cosmetic formulations. *Materials Today: Proceedings*, *22*, 275–280. https://doi.org/10.1016/j.matpr.2019.08.117

Bouillon, G., Daniel, G., Denzer, H., Peppmoller, R., & Franzen, M. (1998). *Abrasive in* *cosmetic products, process for their production and uses thereof*. Google Patents.

Bubakir, M. M., Li, H., Barhoum, A., & Yang, W. (2019). Advances in Melt Electrospinning Technique. In *Handbook of Nanofibers* (pp. 125–156). Springer International Publishing. https://doi.org/10.1007/978-3-319-53655-2_8

Buffiere, J. (2020). *Low-Molecular-Weight Nanocellulose Produced Using Supercritical Water Treatment*. Aalto University.

Cheeveewattanagul, N., Morales-Narváez, E., Hassan, A. R. H. A., Bergua, J. F., Surareungchai, W., Somasundrum, M., & Merkoçi, A. (2017). Straightforward Immunosensing Platform Based on Graphene Oxide-Decorated Nanopaper: A Highly Sensitive and Fast Biosensing Approach. *Advanced Functional Materials*, *27*(38), 1–8. https://doi.org/10.1002/adfm.201702741

Chevalier, Y., & Bolzinger, M.-A. (2013). Emulsions stabilized with solid nanoparticles: Pickering emulsions. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, *439*, 23–34.

Chung, J. J., Im, H., Kim, S. H., Park, J. W., & Jung, Y. (2020). Toward Biomimetic Scaffolds for Tissue Engineering: 3D Printing Techniques in Regenerative Medicine. *Frontiers in Bioengineering and Biotechnology*, *8*(November), 1–12. https://doi.org/10.3389/fbioe.2020.586406

Costa, R., Gomes, A., Tibolla, H., Menegalli, F. C., Lopes, R., Costa, A. L. R., Gomes, A., Tibolla, H., Menegalli, F. C., & Cunha, R. L. (2018). Cellulose nanofibers from banana peels as a Pickering emulsifier: High-energy emulsification processes. *Carbohydrate Polymers*, *194*, 122–131. https://doi.org/10.1016/j.carbpol.2018.04.001

Dai, J., Chae, M., Beyene, D., Danumah, C., Tosto, F., & Bressler, D. C. (2018). Coproduction of cellulose nanocrystals and fermentable sugars assisted by endoglucanase treatment of wood pulp. *Materials*, *11*(9). https://doi.org/10.3390/ma11091645

Dai, L., Wang, Y., Zou, X., Chen, Z., Liu, H., & Ni, Y. (2020). Ultrasensitive Physical, Bio, and Chemical Sensors Derived from 1-, 2-, and 3-D Nanocellulosic Materials. *Small*, *16*(13), 1–25. https://doi.org/10.1002/smll.201906567

de Amorim, J. D. P., de Souza, K. C., Duarte, C. R., da Silva Duarte, I., de Assis Sales Ribeiro, F., Silva, G. S., de Farias, P. M. A., Stingl, A., Costa, A. F. S., Vinhas, G. M., & Sarubbo, L. A. (2020). Plant and bacterial nanocellulose: production, properties and applications in medicine, food, cosmetics, electronics and engineering. A review. *Environmental Chemistry Letters*, *18*(3), 851–869. https://doi.org/10.1007/s10311-020-00989-9

de Oliveira Barud, H. G., da Silva, R. R., da Silva Barud, H., Tercjak, A., Gutierrez, J., Lustri, W. R., de Oliveira, O. B., & Ribeiro, S. J. L. (2016). A multipurpose natural and renewable polymer in medical applications: Bacterial cellulose. *Carbohydrate Polymers*, *153*, 406–420. https://doi.org/10.1016/j.carbpol.2016.07.059

Dervisevic, M., Alba, M., Prieto-Simon, B., & Voelcker, N. H. (2020). Skin in the diagnostics game: Wearable biosensor nano- and microsystems for medical diagnostics. *Nano Today*, *30*, 100828. https://doi.org/10.1016/J.NANTOD.2019.100828

Dhali, K., Ghasemlou, M., Daver, F., Cass, P., & Adhikari, B. (2021). A review of nanocellulose as a new material towards environmental sustainability. *Science of The Total Environment*, *775*, 145871. https://doi.org/10.1016/J.SCITOTENV.2021.145871

Divya, Mahapatra, S., Srivastava, V. R., & Chandra, P. (2021). Nanobioengineered sensing technologies based on cellulose matrices for detection of small molecules, macromolecules, and cells. *Biosensors*, *11*(6). https://doi.org/10.3390/bios11060168

Dufresne, A. (2019). Nanocellulose Processing Properties and Potential Applications. *Current Forestry Reports*. https://doi.org/10.1007/s40725-019-00088-1

Effiong, D. E., Uwah, T. O., Jumbo, E. U., & Akpabio, A. E. (2020). Nanotechnology in Cosmetics : Basics , Current Trends and Safety Concerns — A Review. *Advances in Nanoparticles*, *9*(1), 1–22. https://doi.org/10.4236/anp.2020.91001

Espíndola, S. P., Pronk, M., Zlopasa, J., Picken, S. J., & van Loosdrecht, M. C. M. (2021). Nanocellulose recovery from domestic wastewater. *Journal of Cleaner Production*, *280*, 124507. https://doi.org/10.1016/j.jclepro.2020.124507

Fontana, J. D., De Souza, A. M., Fontana, C. K., Torriani, I. L., Moreschi, J. C., Gallotti, B. J., De Souza, S. J., Narcisco, G. P., Bichara, J. A., & Farah, L. F. X. (1990). Acetobacter cellulose pellicle as a temporary skin substitute. *Applied Biochemistry and Biotechnology*, *24–25*(1), 253–264. https://doi.org/10.1007/BF02920250

Fratoddi, I. (2018). *Hydrophobic and Hydrophilic Au and Ag Nanoparticles . Breakthroughs and Perspectives*. https://doi.org/10.3390/nano8010011

Fujisawa, S., Togawa, E., & Kuroda, K. (2017). Nanocellulose-stabilized Pickering emulsions and their applications. *Science and Technology of Advanced Materials*, *18*(1), 1–13. https://doi.org/10.1080/14686996.2017.1401423

Gentile, G., Cocca, M., Avolio, R., Errico, M. E., & Avella, M. (2018). Effect of Microfibrillated Cellulose on Microstructure and Properties of Poly(vinyl alcohol) Foams. *Polymers 2018, Vol. 10, Page 813*, *10*(8), 813. https://doi.org/10.3390/POLYM10080813

Gouda, M., Hebeish, A. A., & Aljafari, A. I. (2014). Synthesis and characterization of novel drug delivery system based on cellulose acetate electrospun nanofiber mats. *Journal of Industrial Textiles*, *43*(3), 319–329. https://doi.org/10.1177/1528083713495250

Gugulothu, D., Barhoum, A., Nerella, R., Ajmer, R., & Bechlany, M. (2018). Fabrication of Nanofibers: Electrospinning and Non-Electrospinning Techniques. In *Handbook of Nanofibers* (pp. 1–34). Springer International Publishing. https://doi.org/10.1007/978-3-319-42789-8_6-2

Hakkarainen, T., Koivuniemi, R., Kosonen, M., Escobedo-Lucea, C., Sanz-Garcia, A., Vuola, J., Valtonen, J., Tammela, P., Mäkitie, A., Luukko, K., Yliperttula, M., & Kavola, H. (2016). Nanofibrillar cellulose wound dressing in skin graft donor site treatment. *Journal of Controlled Release*, *244*, 292–301. https://doi.org/10.1016/J.JCONREL.2016.07.053

Hameed, A., Fatima, R., Malik, K., Muqadas, A., & Fazal-Ur-Rehman, M. (2019). Scope of Nanotechnology in Cosmetics: Dermatology and Skin Care Products. *Journal of Medicinal and Chemical Sciences Review J. Med. Chem. Sci*, *2*(2), 9–16.

Hasan, N., Biak, D. R. A., Kamarudin, S., Radiah, D., Biak, A., Kamarudin, S., Biak, D. R. A., & Kamarudin, S. (2012). Application of bacterial cellulose (BC) in natural facial scrub. *International Journal on Advanced Science, Engineering and Information Technology*, *2*(4), 272–275.

Heath, L., & Thielemans, W. (2010). Cellulose nanowhisker aerogels. *Green Chemistry, 12*(8), 1448–1453. https://doi.org/10.1039/c0gc00035c

Herman, A., Przemysław, A., Wanda, B., & Andrzej, D. (2012). *Essential Oils and Herbal Extracts as Antimicrobial Agents in Cosmetic Emulsion*. https://doi.org/10.1007/s12088-

012-0329-0

Herrmann, A., Haag, R., & Schedler, U. (2021). Hydrogels and Their Role in Biosensing Applications. *Advanced Healthcare Materials*, *10*(11), 1–25. https://doi.org/10.1002/adhm.202100062

J, C., L, T., LM, B., B, H., W, H., T, V., & KJ, B. (2020). The Impact of a Nanocellulose-Based Wound Dressing in the Management of Thermal Injuries in Children: Results of a Retrospective Evaluation. *Life (Basel, Switzerland)*, *10*(9), 1–11. https://doi.org/10.3390/LIFE10090212

Jacek, P., Dourado, F., & Gama, M. (2019). *Molecular aspects of bacterial nanocellulose biosynthesis*. *0*, 1–17. https://doi.org/10.1111/1751-7915.13386

Jeevanandam, J., Barhoum, A., Chan, Y. S., Dufresne, A., & Danquah, M. K. (2018). Review on nanoparticles and nanostructured materials: History, sources, toxicity and regulations. In *Beilstein Journal of Nanotechnology* (Vol. 9, Issue 1, pp. 1050–1074). Beilstein-Institut Zur Forderung der Chemischen Wissenschaften. https://doi.org/10.3762/bjnano.9.98

Jose Chirayil, C., Mathew, L., & Thomas, S. (2014). Review of recent research in nano cellulose preparation from different lignocellulosic fibers. *Reviews on Advanced Materials Science*, *37*(1), 20–28. http://www.ipme.ru/e-journals/RAMS/no_13714/03_13714_cintil.pdf

Journal, A. I., Gencturk, A., Kahraman, E., Güngör, S., Özhan, G., Özsoy, Y., Sarac, A. S., Kahraman, E., Güngör, S., Özhan, G., Özsoy, Y., & Sarac, A. S. (2016). *Polyurethane / hydroxypropyl cellulose electrospun nanofiber mats as potential transdermal drug delivery system : characterization studies and in vitro assays*. *1401*(April).

https://doi.org/10.3109/21691401.2016.1173047

Kalashnikova, I., Bizot, H., Bertoncini, P., Capron, I., Cathala, B., & Capron, I. (2013). Cellulosic nanorods of various aspect ratios for oil in water Pickering emulsions. *Soft Matter*, *9*(3), 952–959. https://doi.org/10.1039/c2sm26472b

Kang, L., Chen, P., Wang, B., Jia, J., Li, J., Zeng, J., Cheng, Z., Gao, W., Xu, J., & Chen, K. (2019). Cellulose nanocrystal dye as reinforcement matrix of lipstick for inhibiting color migration. *Cellulose*, *0123456789*(199). https://doi.org/10.1007/s10570-019-02827-w

Katz, L. M. (2007). Nanotechnology and applications in cosmetics: General overview. *ACS Symposium Series*, *961*, 193–200. https://doi.org/10.1021/bk-2007-0961.ch011

Khan, M. Q., Kharaghani, D., Shahzad, A., Saito, Y., Ogasawara, H., & Kim, I. S. (2019). Fabrication of antibacterial electrospun cellulose acetate/ silver-sulfadiazine nanofibers composites for wound dressings applications. *Polymer Testing*. https://doi.org/10.1016/j.polymertesting.2018.12.015

Kim, C., Kim, D., Kang, S., Marquez, M., & Lak, Y. (2006). *Structural studies of electrospun cellulose nanofibers*. *47*, 5097–5107. https://doi.org/10.1016/j.polymer.2006.05.033

Kim, S. M., Gwak, E. J., Jeong, S. H., Lee, S. M., & Sim, W. J. (2019). *Toxicology and Risk Assessment Toxicity Evaluation of Cellulose Nanofibers (Cnfs) for Cosmetic Industry Application*. *5*(2). https://doi.org/10.23937/2572-4061.1510029

Kiran Pulidindi, H. P. (2020). Nanocellulose market size by product (nano fibrillated cellulose, nanocrystalline cellulose), by application (composites, paper processing, food & beverages, paints & coatings, oil & gas, personal care). *Industry Analysis Report, Regional Outlook, Growth Potential, Price Trend, Competitive Market Share & Forecast, 2026*.

Kolesovs, S., & Semjonovs, P. (2020). Production of bacterial cellulose from whey—current state and prospects. *Applied Microbiology and Biotechnology*, *104*(18), 7723–7730. https://doi.org/10.1007/s00253-020-10803-9

Kontturi, E., Laaksonen, P., Linder, M. B., Nonappa, Gröschel, A. H., Rojas, O. J., & Ikkala, O. (2018). Advanced Materials through Assembly of Nanocelluloses. *Advanced Materials*, *30*(24). https://doi.org/10.1002/adma.201703779

Kralchevsky, P. A., Ivanov, I. B., Ananthapadmanabhan, K. P., & Lips, A. (2005). On the thermodynamics of particle-stabilized emulsions: curvature effects and catastrophic phase inversion. *Langmuir*, *21*(1), 50–63.

Kukrety, A., Singh, R. K., Singh, P., & Ray, S. S. (2018). Comprehension on the Synthesis of Carboxymethylcellulose (CMC) Utilizing Various Cellulose Rich Waste Biomass Resources. *Waste and Biomass Valorization*, *9*(9), 1587–1595. https://doi.org/10.1007/s12649-017-9903-3

Kupnik, K., Primožič, M., Kokol, V., & Leitgeb, M. (2020). Nanocellulose in drug delivery and antimicrobially active materials. *Polymers*, *12*(12), 1–40. https://doi.org/10.3390/polym12122825

Kushwaha, N., Minocha, N., & Kumar, N. (2020). Use of Nanotechnology in Cosmeceuticals : A Review. *International Journal of Pharmaceutical Science Invention*, *9*(I), 43–51.

Li, M. C., Wu, Q., Song, K., Lee, S., Yan, Q., & Wu, Y. (2015). Article CELLULOSE NANOPARTICLES : STRUCTURE- MORPHOLOGY-RHEOLOGY RELATIONSHIP School of Renewable Natural Resources , Louisiana State University AgCenter , Baton Rouge , Department of Forest Products , Korea Forest Research

Institute , Seoul , 130-712 , K. *ACS Sustainable Chemistry & Engineering*.

Lin, N., Tang, J., Dufresne, A., & Tam, M. K. C. (2019). *Advanced Functional Materials from Nanopolysaccharides*. Springer.

Long, Y., Yan, X., Wang, X., Zhang, J., & Yu, M. (2019). Chapter 2 - Electrospinning: The Setup and Procedure. In *Electrospinning: Nanofabrication and Applications*. Elsevier Inc. https://doi.org/10.1016/B978-0-323-51270-1.00002-9

Lopes, V. R., Sanchez-martinez, C., Strømme, M., & Ferraz, N. (2017). In vitro biological responses to nanofibrillated cellulose by human dermal , lung and immune cells : surface chemistry aspect. *Particle and Fibre Toxicology*, 1–13. https://doi.org/10.1186/s12989-016-0182-0

Lu, X., Zhang, H., Li, Y., & Huang, Q. (2018). Food Hydrocolloids Fabrication of milled cellulose particles-stabilized Pickering emulsions. *Food Hydrocolloids*, *77*, 427–435. https://doi.org/10.1016/j.foodhyd.2017.10.019

Meftahi, A., Khajavi, R., Rashidi, A., Rahimi, M. K., & Bahador, A. (2018). Preventing the collapse of 3D bacterial cellulose network via citric acid. *Journal of Nanostructure in Chemistry*, *8*(3), 311–320. https://doi.org/10.1007/s40097-018-0275-4

Mellou, F., Varvaresou, A., & Papageorgiou, S. (2019). Renewable sources: applications in personal care formulations. *International Journal of Cosmetic Science*, *41*(6), 517–525. https://doi.org/10.1111/ics.12564

Mendoza, L., Batchelor, W., Tabor, R. F., & Garnier, G. (2018). Gelation mechanism of cellulose nanofibre gels: A colloids and interfacial perspective. *Journal of Colloid and Interface Science*, *509,* 39–46. https://doi.org/10.1016/j.jcis.2017.08.101

Meyabadi, F., Dadashian, T., Sadeghi, F. M. M., & Asl, G. E. Z. H. (2014). Spherical cellulose nanoparticles preparation from waste cotton using a green method. *Powder Technology*, *261*, 232–240. https://doi.org/10.1016/j.powtec.2014.04.039

Miguel, S. P., Figueira, D. R., Simões, D., Ribeiro, M. P., Coutinho, P., Ferreira, P., & Correia, I. J. (2018). Electrospun polymeric nanofibres as wound dressings: A review. *Colloids and Surfaces B: Biointerfaces*, *169*, 60–71. https://doi.org/10.1016/j.colsurfb.2018.05.011

Mihranyan, A., Ferraz, N., & Strømme, M. (2012). Current status and future prospects of nanotechnology in cosmetics. *Progress in Materials Science*, *57*(5), 875–910. https://doi.org/10.1016/j.pmatsci.2011.10.001

Mishra, D., Shanker, K., & Khare, P. (2020). Nanocellulose-mediated fabrication of sustainable future materials. In *Sustainable Nanocellulose and Nanohydrogels from Natural Sources* (pp. 217–236). Elsevier. https://doi.org/https://doi.org/10.1016/B978-0-12-816789-2.00010-9

Mitura, S., Sionkowska, A., & Jaiswal, A. (2020). Biopolymers for hydrogels in cosmetics: review. *Journal of Materials Science: Materials in Medicine*, *31*(6). https://doi.org/10.1007/s10856-020-06390-w

Mohite, B. V., & Patil, S. V. (2014). A novel biomaterial: Bacterial cellulose and its new era applications. In *Biotechnology and Applied Biochemistry* (Vol. 61, Issue 2). https://doi.org/10.1002/bab.1148

Mohiuddin, A. K. (2019). An extensive review of cosmetics in use. *Am J Dermatol Res Rev*, *2*, 7.

Morais, F. P., Simões, R. M. S., & Curto, J. M. R. (2020). Biopolymeric Delivery Systems for Cosmetic Applications Using Chlorella vulgaris Algae and Tea Tree Essential Oil. *Polymers 2020, Vol. 12, Page 2689*, *12*(11), 2689. https://doi.org/10.3390/POLYM12112689

Nafisi, S., & Maibach, H. I. (2017). Nanotechnology in cosmetics. In *Cosmetic Science and Technology: Theoretical Principles and Applications*. https://doi.org/10.1016/B978-0-12-802005-0.00022-7

Nissilä, T., Wei, J., Geng, S., Teleman, A., & Oksman, K. (2021). Ice-Templated Cellulose Nanofiber Filaments as a Reinforcement Material in Epoxy Composites. *Nanomaterials 2021, Vol. 11, Page 490*, *11*(2), 490. https://doi.org/10.3390/NANO11020490

Online, V. A., Malik, S., Saha, R., Saha, B., De, S., Malik, S., Ghosh, A., Saha, R., & Saha, B. (2015). A review on natural surfactants. *RSC Advances*, *5*(81), 65757–65767. https://doi.org/10.1039/C5RA11101C

Orlando, I., Basnett, P., Nigmatullin, R., Wang, W., Knowles, J. C., & Roy, I. (2020). Chemical Modification of Bacterial Cellulose for the Development of an Antibacterial Wound Dressing. *Frontiers in Bioengineering and Biotechnology*, *8*(September), 1–19. https://doi.org/10.3389/fbioe.2020.557885

Oun, A. A., Shankar, S., & Rhim, J. (2019). Multifunctional nanocellulose / metal and metal oxide nanoparticle hybrid nanomaterials. *Critical Reviews in Food Science and Nutrition*, *0*(0), 1–26. https://doi.org/10.1080/10408398.2018.1536966

Pacheco, G., de Mello, C. V., Chiari-Andréo, B. G., Isaac, V. L. B., Ribeiro, S. J. L., Pecoraro, É., & Trovatti, E. (2018). Bacterial cellulose skin masks—Properties and sensory tests. *Journal of Cosmetic Dermatology*, *17*(5), 840–847. https://doi.org/10.1111/jocd.12441

Panchal, P., & Mekonnen, T. H. (2019). Tailored cellulose nanocrystals as a functional ultraviolet absorbing nanofiller of epoxy polymers. *Nanoscale Advances*, *1*(7), 2612–2623. https://doi.org/10.1039/C9NA00265K

Pastrana, H., Avila, A., & Tsai, C. S. J. (2018). Nanomaterials in Cosmetic Products: the Challenges with regard to Current Legal Frameworks and Consumer Exposure. *NanoEthics*, *12*(2), 123–137. https://doi.org/10.1007/s11569-018-0317-x

Paximada, P., Tsouko, E., Kopsahelis, N., Koutinas, A. A., & Mandala, I. (2016). Bacterial cellulose as stabilizer of o/w emulsions. *Food Hydrocolloids*, *53*, 225–232.

Perugini, P., Bleve, M., Cortinovis, F., & Colpani, A. (2018). Biocellulose masks as delivery systems: A novel methodological approach to assure quality and safety. *Cosmetics*, *5*(4). https://doi.org/10.3390/cosmetics5040066

Portela, R., Leal, C. R., Almeida, P. L., & Sobral, R. G. (2019). Bacterial cellulose: a versatile biopolymer for wound dressing applications. *Microbial Biotechnology*, *12*(4), 586–610. https://doi.org/10.1111/1751-7915.13392

Press, D. (2011). *Effects of a cellulose mask synthesized by a bacterium on facial skin characteristics and user satisfaction*. 77–81.

Pyrgiotakis, G., Luu, W., Zhang, Z., Vaze, N., DeLoid, G., Rubio, L., Graham, W. A. C., Bell, D. C., Bousfield, D., & Demokritou, P. (2018). Development of high throughput, high precision synthesis platforms and characterization methodologies for toxicological studies of nanocellulose. *Cellulose*, *25*(4), 2303–2319.

Qi, Y., Zhang, H., Xu, D., He, Z., Pan, X., & Gui, S. (2020). Screening of Nanocellulose from Different Biomass Resources and Its Integration for Hydrophobic Transparent Nanopaper. *Molecules*, *25*(1), 1–9.

Ribeiro, A. S., Costa, S. M., Ferreira, D. P., Calhelha, R. C., Barros, L., Stojković, D., Soković, M., Ferreira, I. C. F. R., & Fangueiro, R. (2021). Chitosan/nanocellulose electrospun fibers with enhanced antibacterial and antifungal activity for wound dressing applications. *Reactive and Functional Polymers, 159,* 104808. https://doi.org/10.1016/J.REACTFUNCTPOLYM.2020.104808

Rizzi, V., Gubitosa, J., Fini, P., & Cosma, P. (2021). Neurocosmetics in Skincare—The Fascinating World of Skin–Brain Connection: A Review to Explore Ingredients, Commercial Products for Skin Aging, and Cosmetic Regulation. *Cosmetics 2021, Vol. 8, Page 66*, *8*(3), 66. https://doi.org/10.3390/COSMETICS8030066

Rodríguez, K., Sundberg, J., Gatenholm, P., & Renneckar, S. (2014). Electrospun nanofibrous cellulose scaffolds with controlled microarchitecture. *Carbohydrate Polymers*, *100*, 143–149. https://doi.org/10.1016/j.carbpol.2012.12.037

Roman, M. (2015). Toxicity of cellulose nanocrystals: A review. *Industrial Biotechnology*, *11*(1), 25–33. https://doi.org/10.1089/ind.2014.0024

Samyn, P., Barhoum, A., Öhlund, T., & Dufresne, A. (2018). Review: nanoparticles and nanostructured materials in papermaking. *Journal of Materials Science*, *53*(1), 146–184. https://doi.org/10.1007/s10853-017-1525-4

Santos, A., F, M., A, S., I, P., JAD, S., M, P.-S., F, V., & A, R. (2019). Nanotechnology for the development of new cosmetic formulations. *Expert Opinion on Drug Delivery*, *16*(4), 313–330. https://doi.org/10.1080/17425247.2019.1585426

Selulosa, A. (2019). *Electrospun Cellulose Fibres and Applications*. *48*(7), 1459–1472.

Sfiligoj, M., Hribernik, S., Stana, K., & Kree, T. (2013). Plant Fibres for Textile and Technical Applications. *Advances in Agrophysical Research*.

https://doi.org/10.5772/52372

Sharma, N., Singh, S., Kanojia, N., Grewal, A. S., & Arora, S. (2018). Nanotechnology: A Modern Contraption in Cosmetics and Dermatology. *Applied Clinical Research, Clinical Trials and Regulatory Affairs*, *5*(3), 147–158. https://doi.org/10.2174/2213476x05666180528093905

Sharma, S., Zhang, X., Nair, S. S., Ragauskas, A., Zhu, J., Deng, Y., Yang, J., Dufresne, A., Kalyva, M., Sabella, S., Pompa, P. P., Cingolani, R., & Athanassiou, A. (2014). Thermally enhanced high performance cellulose nano fibril barrier membranes. *RSC Adv.*, *4*(85), 45136–45142. https://doi.org/10.1039/C4RA07469F

Silva, R. R., Raymundo-Pereira, P. A., Campos, A. M., Wilson, D., Otoni, C. G., Barud, H. S., Costa, C. A. R., Domeneguetti, R. R., Balogh, D. T., Ribeiro, S. J. L., & Oliveira, O. N. (2020a). Microbial nanocellulose adherent to human skin used in electrochemical sensors to detect metal ions and biomarkers in sweat. *Talanta*, *218*(May), 121153. https://doi.org/10.1016/j.talanta.2020.121153

Silva, R. R., Raymundo-Pereira, P. A., Campos, A. M., Wilson, D., Otoni, C. G., Barud, H. S., Costa, C. A. R., Domeneguetti, R. R., Balogh, D. T., Ribeiro, S. J. L., & Oliveira, O. N. (2020b). Microbial nanocellulose adherent to human skin used in electrochemical sensors to detect metal ions and biomarkers in sweat. *Talanta*, *218*, 121153. https://doi.org/10.1016/J.TALANTA.2020.121153

Singh, S., Pandey, S. K., & Vishwakarma, N. (2020). Functional nanomaterials for the cosmetics industry. In *Handbook of Functionalized Nanomaterials for Industrial Applications*. INC. https://doi.org/10.1016/b978-0-12-816787-8.00022-3

Singh, T. G., & Sharma, N. (2016). Nanobiomaterials in cosmetics: Current status and future prospects. In *Nanobiomaterials in Galenic Formulations and Cosmetics: Applications of Nanobiomaterials*. Elsevier Inc. https://doi.org/10.1016/B978-0-323-42868-2.00007-3

Soodeh, S., Jhamak, N., Azadeh, G., & Neda, S. (2020). Carboxymethyl cellulose-human hair keratin hydrogel with controlled clindamycin release as antibacterial wound dressing. *International Journal of Biological Macromolecules*, *147*, 1239–1247. https://doi.org/10.1016/J.IJBIOMAC.2019.09.251

Souto, E. B., Fernandes, A. R., Martins-Gomes, C., Coutinho, T. E., Durazzo, A., Lucarini, M., Souto, S. B., Silva, A. M., & Santini, A. (2020). Nanomaterials for skin delivery of cosmeceuticals and pharmaceuticals. *Applied Sciences (Switzerland)*, *10*(5), 1–24. https://doi.org/10.3390/app10051594

Sunasee, R., Hemraz, U. D., & Ckless, K. (2016). Cellulose nanocrystals: a versatile nanoplatform for emerging biomedical applications. *Expert Opinion on Drug Delivery*, *13*(9), 1243–1256. https://doi.org/10.1080/17425247.2016.1182491

Suwannateep, N., Meechaisue, C., & Ruch, H. (2015). *Electrospun Cellulose Acetate Fiber Containing Rubber Extract*. *1119*, 329–333. https://doi.org/10.4028/www.scientific.net/AMR.1119.329

Tan, K., Barhoum, A., Pan, S., & Danquah, M. (2018). Risks and toxicity of nanoparticles and nanostructured materials. In *Emerging Applications of Nanoparticles and Architecture Nanostructures* (pp. 121–139). https://www.sciencedirect.com/science/article/pii/B9780323512541000051

Tang, C., Chen, Y., Luo, J., Low, M. Y., Shi, Z., Tang, J., Zhang, Z., Peng, B., & Tam, K. C. (2019). Pickering emulsions stabilized by hydrophobically modified nanocellulose containing various structural characteristics. *Cellulose*, *26*(13–14), 7753–7767.

https://doi.org/10.1007/s10570-019-02648-x

Tang, C., Spinney, S., Shi, Z., Tang, J., Peng, B., Luo, J., & Tam, K. C. (2018). Amphiphilic Cellulose Nanocrystals for Enhanced Pickering Emulsion Stabilization. *Langmuir*, *34*(43), 12897–12905. https://doi.org/10.1021/acs.langmuir.8b02437

Tang, J., He, H., Wan, R., Yang, Q., Luo, H., Li, L., & Xiong, L. (2021). Cellulose Nanocrystals for Skin Barrier Protection by Preparing a Versatile Foundation Liquid. *ACS Omega*, *6*(4), 2906–2915. https://doi.org/10.1021/acsomega.0c05257

Taylor, P., & Frey, M. W. (2008). *Electrospinning Cellulose and Cellulose Derivatives Electrospinning Cellulose and Cellulose Derivatives*. *March 2013*, 37–41. https://doi.org/10.1080/15583720802022281

Thomas, B., Raj, M. C., Athira, B. K., Rubiyah, H. M., Joy, J., Moores, A., Drisko, G. L., & Sanchez, C. (2018). Nanocellulose, a Versatile Green Platform: From Biosources to Materials and Their Applications. In *Chemical Reviews* (Vol. 118, Issue 24, pp. 11575–11625). American Chemical Society. https://doi.org/10.1021/acs.chemrev.7b00627

Tortorella, S., Buratti, V. V., Maturi, M., Sambri, L., Franchini, M. C., & Locatelli, E. (2020). Surface-modified nanocellulose for application in biomedical engineering and nanomedicine: A review. *International Journal of Nanomedicine*, *15*, 9909–9937. https://doi.org/10.2147/IJN.S266103

Trache, D., Tarchoun, A. F., Derradji, M., Hamidon, T. S., Masruchin, N., Brosse, N., Hussin, M. H., Kupnik, K., Primožič, M., Kokol, V., & Leitgeb, M. (2020). Nanocellulose: From Fundamentals to Advanced Applications. In *Frontiers in Chemistry* (Vol. 8, Issue May). https://doi.org/10.3389/fchem.2020.00392

Uddin, I., Thomas, S., Mishra, R. K., & Asiri, A. M. (2019). Sustainable polymer composites and nanocomposites. In *Sustainable Polymer Composites and Nanocomposites*. https://doi.org/10.1007/978-3-030-05399-4

Ullah, H., Santos, H. A., & Khan, T. (2016). Applications of bacterial cellulose in food, cosmetics and drug delivery. *Cellulose*, *23*(4), 2291–2314. https://doi.org/10.1007/s10570-016-0986-y

Vecino, X., Cruz, J. M., Moldes, A. B., & Rodrigues, L. R. (2017). Biosurfactants in cosmetic formulations: trends and challenges. *Critical Reviews in Biotechnology*, *37*(7), 911–923. https://doi.org/10.1080/07388551.2016.1269053

Ventura, C., Pinto, F., Lourenço, A. F., Ferreira, P. J. T., Louro, H., & Silva, M. J. (2020). On the toxicity of cellulose nanocrystals and nanofibrils in animal and cellular models. In *Cellulose* (Vol. 27, Issue 10). https://doi.org/10.1007/s10570-020-03176-9

Wang, X., Wang, Q., & Xu, C. (2020). Nanocellulose-based inks for 3d bioprinting: Key aspects in research development and challenging perspectives in applications—a mini review. *Bioengineering*, *7*(2). https://doi.org/10.3390/bioengineering7020040

Wang, Z., Liu, Y., Wang, Z., Huang, X., & Huang, W. (2021). Hydrogel-based composites: Unlimited platforms for biosensors and diagnostics. *View*, *March*, 20200165. https://doi.org/10.1002/viw.20200165

Wu, J., & Ma, G. (2016). *Recent Studies of Pickering Emulsions : Particles Make the Difference*. 1–16. https://doi.org/10.1002/smll.201600877

Wulandari, W. T., Rochliadi, A., & Arcana, I. M. (2016). Nanocellulose prepared by acid hydrolysis of isolated cellulose from sugarcane bagasse. *IOP Conference Series: Materials Science and Engineering*, *107*(1). https://doi.org/10.1088/1757-899X/107/1/012045

Xu, C., Zhang Molino, B., Wang, X., Cheng, F., Xu, W., Molino, P., Bacher, M., Su, D., Rosenau, T., Willför, S., & Wallace, G. (2018). 3D printing of nanocellulose hydrogel scaffolds with tunable mechanical strength towards wound healing application. *Journal of Materials Chemistry B, 6*(43), 7066–7075. https://doi.org/10.1039/c8tb01757c

Xu, H., Xie, Y., Zhu, E., Liu, Y., Shi, Z., Xiong, C., & Yang, Q. (2020). Supertough and ultrasensitive flexible electronic skin based on nanocellulose/sulfonated carbon nanotube hydrogel films. *Journal of Materials Chemistry A, 8*(13), 6311–6318. https://doi.org/10.1039/d0ta00158a

Yadav, S., Illa, M. P., Rastogi, T., & Sharma, C. S. (2016). High absorbency cellulose acetate electrospun nanofibers for feminine hygiene application. *Applied Materials Today*, *4*, 62–70. https://doi.org/10.1016/j.apmt.2016.07.002

Yassin, M. A., Gad, A. A. M., Ghanem, A. F., & Abdel Rehim, M. H. (2019). Green synthesis of cellulose nanofibers using immobilized cellulase. *Carbohydrate Polymers*, *205*, 255–260. https://doi.org/10.1016/j.carbpol.2018.10.040

Zhang, J., Elder, T. J., Pu, Y., Ragauskas, A. J., Zhang, F., Ren, H., Tong, G., & Deng, Y. (2007). Facile synthesis of spherical cellulose nanoparticles. *Carbohydrate Polymers*, *69*(3), 607–611. https://doi.org/10.1016/j.carbpol.2007.01.019

Zhang, K., Barhoum, A., Xiaoqing, C., Li, H., & Samyn, P. (2019). Cellulose Nanofibers: Fabrication and Surface Functionalization Techniques. In *Handbook of Nanofibers* (pp. 409–449). Springer International Publishing. https://doi.org/10.1007/978-3-319-53655-2_58

Zhang, T., Zuo, T., Hu, D., & Chang, C. (2017). Dual Physically Cross-Linked Nanocomposite Hydrogels Reinforced by Tunicate Cellulose Nanocrystals with High

Toughness and Good Self-Recoverability. *ACS Applied Materials and Interfaces*, *9*(28), 24230–24237. https://doi.org/10.1021/acsami.7b06219

Zhao, D., Zhu, Y., Cheng, W., Chen, W., Wu, Y., & Yu, H. (2021). Cellulose-Based Flexible Functional Materials for Emerging Intelligent Electronics. *Advanced Materials*, *33*(28), 1–18. https://doi.org/10.1002/adma.202000619