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EXPLORING ONION PEEL (ALLIUM CEPA) DERIVED HERBAL NANOCELLULOSE AS A GREEN NANOCARRIER FOR ANTI-INFLAMMATORY PROPERTIES: A COMPREHENSIVE REVIEW

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ABSTRACT

Inflammation leads to many chronic and acute diseases. This shows the need for safer and more effective drug delivery methods. This review looks at onion peel (allium cepa l.) As a rich source of bioactive compounds, such as quercetin, kaempferol, ferulic acid, and vanillic acid. It also investigates the use of nanocellulose from herbal and plant-based sources as an eco-friendly carrier for these anti-inflammatory compounds. Nanocellulose includes cellulose nanocrystals (CNCs), cellulose nanofibers (CNFs), and bacterial nanocellulose (BNC). It is biocompatible, has a large surface area, is biodegradable, and has surface chemistry that can be modified for better drug loading and stability. We examine the main inflammatory markers used for diagnosis and monitoring. We also discuss the pharmacological profile of the bioactive in onion peel and review green extraction methods. This review provides a strong scientific foundation for researchers exploring green nanotechnology, onion peel valorization, and herbal anti-inflammatory drug delivery.

KEYWORDS: Green nanotechnology, herbal nanocellulose, onion peel, anti-inflammatory, quercetin, bioavailability, cellulose nanocrystals, cellulose nanofibers.

INTRODUCTION

Inflammation is a critical biological reaction to harm the tissue, infection, or illness. Acute inflammation gives out as a protective mechanism; however, chronic inflammation add up to the primary pathophysiology of various impairing diseases, including rheumatoid arthritis, inflammatory bowel disease, neurodegenerative disorders, cardiovascular diseases, type 2 diabetes, and several cancers.[1,2] The global toll of inflammatory diseases is still rapidly increasing, and non-communicable diseases are being accountable for greater than 71% of all deaths.[3] Ordinary anti-inflammatory drugs such as nsaids and corticosteroids work well, but they can cause after effects like gastrointestinal toxicity, nephrotoxicity, and immune suppression when used for a long time.[4,5]onion (allium cepa l.) And particularly its peel, which is the outermost dry layer that is normally tossed away as agricultural waste, is an incredibly rich, low-cost, and underutilized origin of bioactive phytochemicals. Onion peel contains heavy amount of quercetin, kaempferol, ferulic acid, vanillic acid, and other flavonoid glycosides. These are all known to be anti-inflammatory, antioxidant, antimicrobial, and good for the liver.[6,7] Modifying onion peel waste into functional pharmaceutical nanomaterials is a phenomenal example of how circular economy and zero-waste ideas can work in combination. Onion peel obtain phytochemicals have stunning pharmacological outline, but they have serious pharmacokinetic problems, such as poor water solubility, rapid metabolic degradation, low oral bioavailability, and instability under physiological conditions.[8,9]

Nanocellulose provides a sophisticated solution by encapsulating bioactive within carrier systems that safeguard them from degradation, improve bioavailability, allow for controlled release, and promote targeted delivery.[10,11]

Nanocellulose comes from the most general biopolymer present on earth, has a unique set of properties: it has a high aspect ratio and an remarkable mechanical strength, a large surface area, outstanding water holding capacity, biodegradability, and low cytotoxicity.[12,13] Herbal nanocellulose, sourced from onion peel and other medicinal plants, signifies a transformative shift towards 'green nanotechnology,' merging sustainable chemistry with biomedical engineering.[14,15] From 2020 to 2022, the number of scientific papers on nanocellulose in drug delivery applications grew by about 60%.[16]

2. MATERIALS AND METHODS

This study is based on an extensive review of previously published literature sourced from google scholar, pubmed, scopus, springer, nature, researchgate, and standard reference books.

3. Classification and structural properties of nanocellulose

There are generally three main types of nanocellulose and they are: cellulose nanocrystals (cncs), cellulose nanofibers (cnfs), and bacterial nanocellulose (bnc).[17,18] These groups are classified on the basis on where they originate from, how they are made, their shape, and their physical and chemical properties.

3.1 cellulose nanocrystals (cncs)

These cellulose nanocrystals are for the most part made by controlled acid hydrolysis of cellulose-rich sources. This procedure critically breaks down amorphous areas while keeping crystalline areas untouched, therefore this results in rigid and needle like nanoparticles.[19,20] Cncs derived from plants usually have diameters between 5 to 30 nm and lengths between 100 to 500 nm.[21,22] The crystallinity index is usually between 54 and 88%. Hydrolysis with sulphuric acid adds negatively charged sulphate ester groups to the surface of the cnc, making it stable in colloids and easy to disperse in water.[23] After the flavonoid-rich outer layers are taken off, onion peel cellulose is a great source for cnc extraction using standard alkali and bleaching pretreatments.[24]

3.2 Cellulose nanofibers (cnfs)

Cellulose nanofibers are typically made by mechanically defibrillating cellulose, which is generally done prior to or succeeding chemical or enzymatic pretreatments.[25,26] Cnfs contains both amorphous and crystalline sectors, due to which it gives them a semi-crystalline network structure with a diameters of 1 to 100 nm and lengths of several micro meters.[27] The tempo oxidation pretreatment selectively changes c6 primary hydroxyl groups into carboxyl groups. This makes defibrillation uncomplicated and adds surface charge.[28,29] Because cnfs have a high aspect ratio and can form networks, they are ideal for carry onion peel extracts like quercetin and kaempferol in hydrogels.[30]

3.3 Bacterial nanocellulose (bnc)

Few types of bacteria, like gluconacetobacter xylinus and pseudomonas spp., make bacterial nanocellulose exterior of their cells.[31,32] Bnc, on the other side, it does not need any kind of chemical purification to get rid of lignin or hemicellulose. This makes a three-dimensional nanofibrous hydrogel that is unadulterated and crystalline.[33] Bnc nanofibers have diameters of 20–100 nm and are potent, hold a lot of water content, and are safe for living things. If the concentration increases more than 1000 µg/ml, then the cytotoxicity studies have shown that it is not safe and is harmful.[34]

4. Inflammatory markers: relevance to anti-inflammatory research

Inflammatory markers, termed as acute-phase reactants, are biochemical indicators whose measures may vary markedly in response to inflammation. These markers are clinically required for diagnosing inflammatory conditions, monitoring disease progression, evaluate treatment potency, and alarming the therapeutic decisions, including antibiotic ceasing and sepsis evaluation.[35] In the domain of herbal nanocellulose-based anti-inflammatory research, these biomarkers function as quantitative endpoints in in vitro assays, in vivo models, and clinical trials. In clinical practice, the three most commonly measured non-specific inflammatory markers are procalcitonin (pct), erythrocyte sedimentation rate (esr), and c-reactive protein (crp). These markers, when used together, can reliably tell if someone is inflamed and keep track of anti-inflammatory treatments, such as those based on quercetin-loaded onion peel-derived nanocellulose formulations.

Table 1 below summarizes the key inflammatory markers most relevant to nanocarrier-based anti-inflammatory research, their biological descriptions, and their diagnostic/monitoring roles.

Table 1: Key inflammatory markers used in nanocarrier-based research.

Marker	Description	Role in diagnosis/monitoring	Reference
C-reactive protein (crp)	Crp is a pentameric protein (~115 kda) produced by the liver when inflammation occurs.[83]	Crp cannot differentiate between cause and effect of a disease; its diagnostic use depends on clinical interpretation. Monitors inflammatory burden in quercetin therapy.[85]	[83,84]
Erythrocyte sedimentation rate (esr)	Esr is a blood test measuring the sedimentation rate of rbcs in a test tube.[86]	Esr cannot confirm a specific disease but indicates general inflammation. Used alongside physical exams and other tests for differential diagnosis.[87]	[86,87]
Procalcitonin (pct)	Pct is an inflammatory marker used to detect severe bacterial infections.[88]	Pct detects symptoms in their latent stage; its level monitoring is important in sepsis and antibiotic stewardship decisions.[89]	[88,89]

5. Taxonomical identification of *allium cepa* (onion)

Allium cepa l. Is the member of the plantae kingdom and is part of the amaryllidaceae family, the allium genus, and the cepa species. It is one of the oldest and most widely grown bulb crops in the world. It has been used as food and medicine since ancient egypt, greece, and china. The word "onion" comes from the latin word unio, which means "single large pearl." this is because the plant has only one bulb. The plant is herbaceous and lives for two years, but it is usually grown as an annual crop. This crop grows in many temperate and subtropical areas around the world, and india is one of the top producers and consumers of it.[36,37]

5.1. Microscopical description

When you look at the onion bulb scales (allium cepa) under a microscope, you can see that the cells are arranged in a way that is different in the outer dry (tunica) and inner fleshy layers. The onion peel is the brown, papery skin on the outside. It is made up of many layers of dead, compressed epidermal cells with thickened, lignified cell walls. These cells are long and shaped like polygons. They are tightly packed together with no spaces between them, and they stain strongly with safranin because they have a lot of phenolic and flavonoid compounds in them. When you look at the outer dry scale with a bright-field microscope, you can see that the epidermal layer has straight-walled rectangular cells. The dry peel layers usually don't have stomata, which sets them apart from the green aerial parts.

The mesophyll cells in the inner fleshy scales have big parenchymatous cells with thin cellulosic walls, big nuclei, and big vacuoles that store sugars and flavonoid glycosides. Vascular bundles are collateral and are spread out throughout the fleshy scale tissue.[38]

When seen under polarized light microscopy, the cellulose microfibrils in the cell walls of onion peels show strong birefringence. This confirms that the cellulose chains are arranged in a highly ordered, crystalline way, which is an important quality that makes onion peel a good source of high-quality nanocellulose. There are also calcium oxalate crystals and starch granules in the parenchymatous cells of the peel tissue. Histochemical staining with phloroglucinol-hcl implies that lignin is present in the outer layers, and lugol's iodine solution shows that starch is present in the inner layers.[39,40]

The onion peel has a multilayered cell wall. The primary cell wall is made up of a lot of pectin, hemicellulose, and cellulose. The secondary wall in mature outer scale cells has more cellulose in it. This hierarchical structure of cellulose in the cell walls of the peel is what makes it possible to get nanocellulose through chemical or mechanical means. Studies using atomic force microscopy and transmission electron microscopy on isolated onion peel nanocellulose have shown needle-like or rod-shaped nanocrystals (cncs) with widths of about 5–20 nm and lengths of 100 to 500 nm. These nanocrystals have a high aspect ratio, which makes them good for making nanocarriers.[41,42]

5.2. Morphological description

Allium cepa is a biennial herb that is commercially cultivated as an annual. It is an erect, glabrous plant, typically 25–100 cm in height. Its morphological features are summarized in table 2 below.

Table 2: morphological characteristics of *allium cepa* (onion).

S. No.	Part	Description	Shape	Size	Reference
1	Bulb	The edible bulb is a altered underground stem comprise of a compressed disc-like base bordering by multiple concentric plump leaf bases (scales). The outer layers form the characteristic dry, papery peel, which are brown, red, or yellow in color depending on the variety.	Globose to ovoid; concentrically layered	4–10 cm in diameter	[36, 43]

2	Leaves	Leaves are generally hollow, cylindrical in shape, and glaucous, arising from the basal disc of the bulb. They are fistular and narrow into a sharp point at the apex.	Hollow, cylindrical, and erect	20–60 cm in length	[36, 44]
3	Roots	The root system is fibrous and adventitious, arising from the basal plate of the bulb. Roots are thin, white, and non-branching at the initial stage. The root system is shallow, typically penetrating to a depth of 30–45 cm in soil.	Fibrous, adventitious	Thin; 30–45 cm depth	[44]
4	Scape (flower stalk)	The flowering stalk is hollow, erect, and slightly swollen near the middle.	Hollow, cylindrical	30–100 cm in height	[36, 45]
5	Flowers	Flowers are small, star-shaped, spherical umbel. Petals are white to pale pink with a greenish midrib. The perianth consists of 6 tepals.	Star-shaped, umbellate	3–5 mm per flower	[45]
6	Onion peel	The outer layer dry, papery layers of bulb, generally implied as the onion peel.	Thin, brittle, papery	Thickness: 0.1–0.3 mm per layer	[39, 46]
7	Seeds	Seeds are small, black, angular, and wrinkled. They are produced within a three-chambered capsule and are used for asexual reproduction.	Angular, wrinkled	2–4 mm	[36, 44]

6. Green extraction and synthesis of herbal nanocellulose from onion peel

Herbal nanocellulose consists of nanocellulose obtained from medicinal plants, aromatic herbs, agro-industrial byproducts, and various non-woody plant materials. Using onion peel (allium cepa l.) As a raw material for extracting nanocellulose is very interesting because it is an abundant agricultural by-product. Onions are one of the most widely grown vegetables in the world, and they produce millions of tons of peel waste each year. At the same time, onion peel is full of anti-inflammatory flavonoids that can work together to make the resulting nanocarrier more effective [47,48]. This approach is based on green synthesis methods that use fewer harmful chemicals, less energy, and have less of an effect on the environment.[49,50]

6.1 onion peel and other herbal plant sources

The dry outermost peel layers of a onion contains cellulose, hemicellulose, and lignin in the cell wall matrix. They also contains a very huge concentration of biologically active flavonoids, especially quercetin and its glycosides, which stay with the cellulose fraction during processing.[51,52] In addition to onion peel, many other plant-based sources have been used to extract nanocellulose. These include sugarcane bagasse, rice husk, wheat straw, cotton linters, banana rachis, pineapple leaf fiber, jute, hemp, and different medicinal plant residues.[53,54] Utilizing agro-industrial waste is consistent with the principles of a circular economy.[55] Nanocellulose has been extracted from vetiveria zizanioides (vetiver) roots, saccharum officinarum (sugarcane), and dendrobium sonia earsakul (orchid) stems, among other botanically notable species.[56,57]

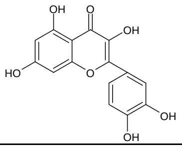
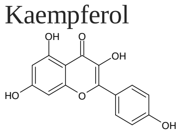
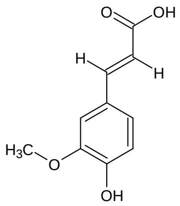
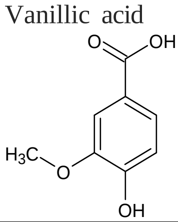
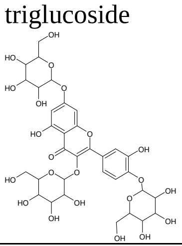
7. Chemical constituents of *allium cepa* (onion peel)

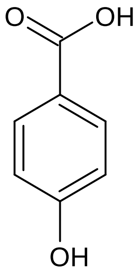
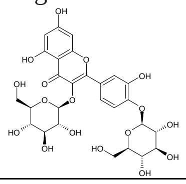
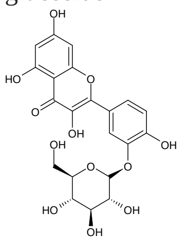
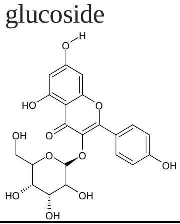
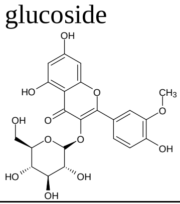
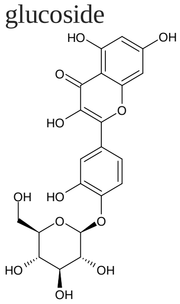
The skin of allium cepa is full of dissimilar biologically active phytochemicals. Even though onion peel is a derivate of industry and agriculture, it has increased levels of flavonoids, phenolics, and few other antioxidants. The leading chemical sections of onion peel, with their chemical structure, molecular formula, molecular weight, and biological activity are listed in table 3.

Quercetin and its glycosides makes upto 85–90% of the total flavonoid content in onion peel. These quercetin derivatives are accountable to a large section of the anti-inflammatory, antioxidant, and anticancer effects that onion peel extracts possess. The outermost peel layers contains abundant amount of quercetin than the edible parts present on the inside, therefore making them a reliable source for use in medicine.[46,58]

The cellulose in onion peel makes up 27% to 35% of the dry weight. It is also made up of hemicellulose (16% to 24%) and lignin (12% to 18%), which together make a strong lignocellulosic matrix. When treated with chemicals (acid hydrolysis or tempo-mediated oxidation), this cellulose becomes nanocellulose in the form of cellulose nanocrystals (cncs) or cellulose nanofibers (cnfs). These are the building blocks of the herbal nanocarrier system suggested in this study.[41,59]

Table 3: Chemical constituents of onion peel.

Sl. No.	Name of the compound	Nature of compound	M.F	M.w. G/mol	Activity
1	Quercetin 	Flavonoid	$C_{15}H_{10}O_7$	302.24	Antioxidant, antifungal, anticarcinogenic, hepatoprotective[100,101]
2	Kaempferol 	Flavonoid	$C_{15}H_{10}O_6$	286.24	Anti-inflammatory[101,102]
3	Ferulic acid 	Phenolic acid	$C_{10}H_{10}O_4$	194.18	Antioxidant[101,103]
4	Vanillic acid 	Phenolic acid	$C_8H_8O_4$	168.15	Antibacterial, antimicrobial, chemo preventive, anti-inflammatory[101,104]
5	Quercetin 3,7,4-triglucoside 	Flavonoid Glycoside	$C_{33}H_{40}O_{22}$	788.7	Antibacterial, anti parasite [101,105]

6	P-hydroxybenzoic acid 	Phenolic compound	$C_7H_6O_3$	138.12	Antimicrobial, antialgal, antimutagenic, antiestrogenic, hypoglycemic, anti-inflammatory, anti-platelet aggregating, nematicidal, antiviral, antioxidant[101,106]
7	Quercetin-7,4-Diglucoside 	Flavonoid	$C_{27}H_{30}O_{17}$	626.5	Antioxidant, anti inflammatory [101,107]
8	Quercetin-3-o-glucoside 	Flavonoid glycoside	$C_{21}H_{20}O_{12}$	464.38	Anti-cytotoxic, antioxidative and anti-inflammatory[101,108,109]
9	Kaempferol-3-o-glucoside 	Flavonoid	$C_{21}H_{20}O_{11}$	448.38	Anti-inflammatory, antioxidant, neuroprotective, cardioprotective, antiobesity, antiosteoporotic, anticancer, antiulcer, and antidiabetic[101,110]
10	Isorhamenti-3-o glucoside 	Flavonoid	$C_{22}H_{22}O_{12}$	478.4	Anti microbial[101,111]
11	Quercetin-4-o-glucoside 	Flavonoid glycoside	$C_{21}H_{20}O_{12}$	464.4	Anti-inflammatory[101,111]

7.1 Quercetin anti-inflammatory

Quercetin is the principal and most pharmacologically significant bioactive compound in onion peel.[60,61] It has strong anti-inflammatory effects because it stops the nf-κb and mapk signalling pathways, which stops the transcription of pro-inflammatory genes and lowers the levels of tnf-α, il-6, and il-1β.[62] Quercetin also stops the enzymatic activity of cyclooxygenase-2 and inducible nitric oxide synthase, which are important parts of the inflammatory cascade at many levels.[63] It also has a strong ability to scavenge free radicals, which lets it neutralise reactive oxygen species that make inflammatory responses stronger. This makes it effective against both oxidative stress and inflammation at the same time.[64] Quercetin has some amazing properties, but its clinical usefulness is very limited because it doesn't dissolve well in water and isn't very bioavailable when taken by mouth. Nanocellulose-based encapsulation solves these problems by making it more soluble, stable, and releasing it in a controlled way.[65,66]

7.2 Kaempferol anti-inflammatory

Kaempferol is the second most important flavonoid in onion peel and is a well-known anti-inflammatory agent.[67] It inhibits the production of pro-inflammatory cytokines such as tnf-α, il-1β, and il-6, and it also stops cox-2 from being expressed at the transcriptional level by interfering with nf-κb activation. This lowers the amount of prostaglandins made at sites of inflammation.[68] Kaempferol also changes how immune cells work by lowering the inflammatory responses caused by macrophages and the release of inflammatory mediators like nitric oxide.[69] Kaempferol-3-o-glucoside, which is found in large amounts in onion peel, has other effects as well, such as protecting the brain, heart, and bones, as well as fighting obesity and diabetes.[70] Kaempferol's low solubility in water is overcome when it is loaded onto nanocellulose carriers, which allows it to be released over time at inflamed tissues[71]

7.3 Ferulic acid antioxidant and anti-inflammatory

Ferulic acid is a hydroxycinnamic acid phenolic compound found in onion peel that has strong antioxidant and anti-inflammatory properties.[72] It stops lipid peroxidation by getting rid of free radicals like hydroxyl, superoxide, and peroxyl radicals. This protects cell membranes from oxidative damage that starts and keeps inflammatory cascades going.[73] Ferulic acid has been demonstrated to inhibit the expression of pro-inflammatory cytokines and diminish the activation of nf-κb, thereby contributing to its anti-inflammatory properties at the molecular level.[74] Its bioavailability, although superior to numerous flavonoids, can be further augmented through nanoencapsulation, which safeguards ferulic acid from swift metabolic conjugation and prolongs its retention at inflamed sites.[75] Combining ferulic acid and quercetin on the same nanocellulose carrier made from onion peel makes a multi-compound formulation that works together to reduce inflammation in different ways.

7.4 Vanillic acid antimicrobial and anti-inflammatory

Vanillic acid is a benzoic acid derivative present in onion peel, exhibiting established antibacterial, antimicrobial, chemo preventive, and anti-inflammatory properties.[76] It has anti-inflammatory effects because it stops the production of inflammatory mediators like prostaglandins and leukotrienes and stops the activation of nf-κb-dependent gene expression in macrophages and other immune cells.[77] Vanillic acid exhibits substantial antioxidant properties by chelating metal ions that facilitate free radical generation, thereby enhancing the ros-scavenging effects of quercetin and ferulic acid within the same onion peel matrix.[78] Its antimicrobial properties against both gram-positive and gram-negative bacteria are especially beneficial in wound healing and infected inflammatory states, providing a dual anti-inflammatory and antimicrobial effect when integrated into nanocellulose-based wound dressings derived from onion peel.[79]

7.5 p-hydroxybenzoic acid and quercetin glycosides

The p-hydroxybenzoic acid found in onion peel has a very wide range of biological effects, including oestrogenic, antimicrobial, antialgal, antimutagenic, hypoglycemic, antiplatelet, antiviral, antioxidant, and anti-inflammatory effects.[80] The quercetin glycosides found in onion peel, such as quercetin-3,7,4-triglucoside, quercetin-3,4-diglucoside, quercetin-7,4-diglucoside, and quercetin-3-o-glucoside, are water-soluble forms of quercetin that are easier for the body to use. They have antioxidant, anti-neuroinflammatory, and oxidative stress management effects.[81]

Isorhamnetin-3-o-glucoside, which is also found in onion peel, adds more anti-inflammatory and antioxidant activity.[82] When these compounds are put on nanocellulose carriers made from onion peel cellulose, the resulting formulation is a complete multi-bioactive system that treats inflammation in many different ways. This leads to better therapeutic results than single-compound formulations.

Table 4 below presents the pharmacological activities of onion peel extracts as reported in the literature, encompassing antimicrobial, antioxidant, and anticancer activities.

Table 4: Pharmacological activity of onion peel (allium cepa l.) Extracts.

S.no.	Activity	Method used	Dose	Key outcomes	Reference
Anti-inflammatory activity					
01	Anti-inflammatory activity (carrageenan-induced paw oedema model)	In vivo	200, 400 mg/kg	Anti-inflammatory and gastric mucosa protective activity	[90]
02	Anti-inflammatory activity(ficus racemosa l)	In vitro	0.01 µg/ml and 0.1 µg/ml.	Anti-inflammatory activity increases.	[91]
Antioxidant activity					
03	Antioxidant activity (dpph radical scavenging)	In vitro (percolation method)	25 – 400 µg/ml	Ic50 value of the extract highest antioxidant activity(ethyl acetate),lowest(water fraction)	[92]
04	Antioxidant and cytoprotective activity (h_2o_2-induced oxidative stress)	In vitro	50 µm (24 hr)	Significant viability drop to 42.79	[93]
Antimicrobial activity					
05	Antimicrobial activity (bacterial strains: s. Aureus, e. Coli, p. Aeruginosa)	In vitro (agar well diffusion)	0.09 mg/ml to 9.0 mg/ml (depending on the cultivar and bacteria strain).	White skin extracts uniquely inhibited pseudomonas aeruginosa (up to 4.0 mm).	[94]
06	Antifungal activity (s. Aureus, s. Epidermidis, p. Aeruginosa, e. Coli, s. Typhimurium, k. Pneumoniae, and c. Albicans.)	In vitro (agar well diffusion method)	50mg/ml (upper test concentration)	key antifungal constituent, bactericidal activity.	[95]

Anticancer activity					
07	Anticancer activity	In vitro	1, 5, 10, 50, 100 µg/ml	Phenols and flavonoids show inhibitory effect on the cancerous cells of stomach, colon, breast and prostate cancer. Quercetin increases the bioavailability of some anticancer medicines like tamoxifen,	[96]
08	Antiproliferative activity (widr cells)	In vitro (mtt assay)	50, 100, 200, and 400 µg/ml	Cytotoxicity increased, ic_{50} of 1363.29 µg/ml	[97]
Antidiabetic activity					
09	Antidiabetic activity (α-glucosidase and α-amylase inhibition)	In vitro	0.1–2 mg/ml (aqueous and ethanolic extracts)	Onion peel extract showed potent α-glucosidase inhibition and moderate α-amylase inhibition ;quercetin and kaempferol identified as primary inhibitory compounds.	[98]
10	Antidiabetic and hepatoprotective activity (stz-induced diabetic rat model)	In vivo	300 mg/kg/day for 28 days	Reduction in blood sugar (via insulin secretion)	[99]

Discussion and future perspective

The current review underlines the important potential of herbal nanocellulose (plant derived) derived from allium cepa peel as an eco-friendly, sustainable, and biocompatible nanocarrier system for anti-inflammatory drug delivery applications. The blend of two important factors the rich phytochemical profile of onion peel (especially quercetin and related flavonoids) and the structural benefits of nanocellulose as a drug delivery matrix makes this system a strong candidate in the fields of herbal pharmacology and nanomedicine.

Standardization and quality control: development of validated analytical techniques (ftir, xrd, tem, and nmr) for characterizing onion peel nanocellulose and creating pharmacopeial standards.

Surface functionalization: design of ph-responsive, thermo-responsive, or receptor-targeted nanocellulose systems that can deliver anti-inflammatory agents directly to inflamed areas.

Co-loading strategies: concurrently loading quercetin with other anti-inflammatory compounds from onion, such as isorhamnetin, kaempferol, and ferulic acid, to create synergistic effects.

In vivo validation: with the help of in vivo studies in established animal models of inflammation, having carrageenan induced paw inflammation, collagen triggered arthritis, and dss induced colitis, to confirm the anti-inflammatory effects of onion peel nanocellulose systems.

Toxicological profiling: detailed evaluations of both acute and sub chronic toxicity, including tests for genotoxicity and immunotoxicity, to ensure the safety of the nanocarrier.

Clinical translation: starting phase clinical trials assessing the treatment's effectiveness.

CONCLUSION

This review shows that onion peel (allium cepa l.) Is a valuable, underused source of both cellulosic biomass and bioactive compounds, especially quercetin, kaempferol, ferulic acid, and vanillic acid. These can be combined into an effective green nanocarrier system for anti-inflammatory treatments. The unique properties of nanocellulose, such as its large surface area, ability to break down naturally, adjustable surface chemistry, and compatibility with living tissues, work well with the anti-inflammatory properties of onion peel flavonoids. This creates a twofold benefit where the carrier also helps enhance the treatment. Key inflammatory markers, including crp, esr, and pct, provide measurable endpoints for assessing the effectiveness of these formulations. Research shows that nanocellulose carriers significantly improve the absorption, stability, and treatment effects of quercetin and other onion peel compounds through various molecular processes, including the inhibition of nf-κb, suppression of cox-2, and scavenging of reactive oxygen species. The plentiful and inexpensive supply of onion peel waste from agriculture, along with the proven safety of nanocellulose, makes this a very promising and sustainable option for future anti-inflammatory therapies.

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