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Review Article

A Comprehensive Review on Oil Palm Fibre Implementations in Medical Sector

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Objective. Reviewing oil palm fibre (OPF) utilisation in various medical sectors. *Background*. The OPF, especially in nanocellulose form, is frequently used due to its exceptional mechanical attributes, considerable surface area, versatility for surface functionalisation, biocompatibility, and nontoxicity. *Method*. Only articles published in the last ten years (2012-2022) and written in English were reviewed in this study. An electronic search was conducted in Google Scholar, ScienceDirect, and PubMed using the terms "oil palm fibres in the medical field" and "oil palm fibre." *Results*. Among the 459 articles obtained, only 24 were accessible as full text and satisfied the parameters set in this study. *Conclusion*. The OPF could be widely employed in the medical domain, particularly the biomedical branch, for drug delivery, tissue engineering, wound dressing, and antimicrobial agent transporters. The substance also demonstrated promising results and significant capacities to be utilised and further studied.

1. Introduction

The oil palm (Figure 1) plantation industry produces palm oil with phytochemical compounds, including tocotrienols, carotenoids, phytosterols, squalene, coenzyme Q_{10}, and phospholipids. It is known to have multiple nutritional, biological, and cosmetic uses [1]. The palm oil plantation industry creates a large amount of oil palm waste (OPW). Oil palm fibre (OPF) was reported as the most prominent product of OPW [2]. The summary of oil palm products and residues is shown in Figure 2.

OPF is usually obtained from parts of the oil palm tree, including the leaves, empty fruit bunch, frond, and trunk [4, 5]. Its fundamental properties depend on the postprocessing technique and the location of the fibre harvested. OPF is a lignocellulosic fibre comprising lignin and cellulose, with percentages of cellulose, hemicellulose, and lignin around 30–60%, 20–40%, and 15–25%, respectively. The most common OPF component used in material development is the fibre derived from oil palm empty fruit bunch (OPEFB) due to its abundance and low price [4]. OPEFB is rich in cellulose, hence a promising material for obtaining nanocellulose and producing cellulose-derived goods. Due to its cellulosic contents, OPEFB might be an excellent material selection compared to other agricultural wastes. The OPEFB fibres are obtained from oil palm fruits via retting, while oil palm mesocarp fibres are generated from waste materials that would be discarded postextraction.

Several reports documented utilising OPF from OPEFB as a resource for cellulose nanofibres (CNF) and cellulose nanocrystal (CNC) procurement [4–7]. Nanocellulose is a new biopolymer category applicable in various interdisciplinary sectors, including biomedical and pharmaceuticals, membranes, three-dimensional (3D) printing, energy appliances, and flexible electronics [6]. Nanocellulose could be classified according to its form and sources: cellulose nanocrystals (CNCs), nanocrystalline cellulose (NCC), cellulose nanowhiskers (CNWs), cellulose nanofibres (CNFs) or nanofibrillated cellulose (NFC), and bacterial nanocellulose (BNC) [6, 7].

The directed procurement of CNCs and CNFs is performed by disintegrating plant substances through chemical or mechanical approaches. Furthermore, nanocellulose is environmentally safe and sustainable; thus, it is an attractive and environmentally friendly alternative for prospective business and academic research. OPF, primarily as nanocellulose, is commonly used in biomedical applications owing to its exceptional mechanical characteristics, significant surface area, versatility for surface functionalisation, biocompatibility, and nontoxicity [6]. Consequently, the present review is aimed at highlighting the employment or possible utilisations of OPF in various medical industries.

2. Method

Electronic searches in Google Scholar, ScienceDirect, and PubMed databases were conducted using "oil palm fibres in the medical field" and "oil palm fibre." Only articles published within the last ten years (2012–2022) were considered in this study. Inclusion criteria include literature in the English language, articles on fibres from oil palm trees, and subjects in the medical field only.

3. Results

The electronic search conducted in this study yielded 459 articles. The papers were then manually assessed for subject pertinence and replications. Duplicate articles were excluded (30); 186 articles were excluded after studying the title, while 62 articles were excluded after reading the abstract, resulting in the exclusion of 278 articles, while 132 publications were considered irrelevant to the current study. Articles in a language other than English were excluded (11). Articles without full-text access were also excluded (14). Eventually, 24 articles were selected for full-text evaluations, which were further discussed. The use of OPF in the medical field was categorised into four categories based on the focus area: drug transportation, tissue engineering, antimicrobial agent bearer, and wound care administration (Table 1).

The focus area in the utilisation of OPF in the medical field includes drug delivery (14), tissue engineering (7), antimicrobial agent bearer (5), and wound care (2). Some of the papers reported multiple focus areas concerning the use of OPF in their study.

4. Discussion

OPF in the form of CNC has been used in the medical industry as reported in many studies as follows.

FIGURE 1: The oil palm tree (*Elaeis guineensis*).

4.1. Drug Transportation. Several publications reported on the employment of CNCs in drug distribution utilisation to regulate drug release rates and the number of drugs in blood circulation, enhancing drug solubility, stability, therapeutic potency and diminishing clearance, negative surface charge and a high specific surface area ratio, and colloidal reliability are among the exceptional attributes of CNCs (Figure 3) [6, 7, 29].

Furthermore, the surfaces of the substance could be functionalised due to hydroxyl groups. The beneficial attributes allow high levels of charged or neutral medications to be stocked on CNCs, thus modulating active ingredient release and conveying genes to determined areas [6, 7, 11, 12].

The hydrophilic characteristics and poor drug-loading behaviour of CNCs restrict the employment of the substance in its pure form. Moreover, some CNC application issues are due to its high surface energy, leading to accumulation and phase dissociation from matrixes during production. The polar chemical groups in CNC elements also lead to dispersion concerns in nonpolar media, thus restraining their characteristics. The substance is also susceptible to absorbing water and thus degrades the mechanical attributes of the substance obtained. The diminished mechanical properties would then lower the compatibility of CNCs with hydrophobic polymers, hindering them from uniformly spreading in any media or matrix [7]. Consequently, the challenges of preserving CNC post alterations must be addressed to augment CNC-based medication transportation approaches [7, 15].

Several studies proposed adjustments to the CNC surface via sulfonation to improve its crystallinity. Sulfonation will destroy its amorphous regions, enhancing hydrophobic medicine attachments due to the reactive functional groups

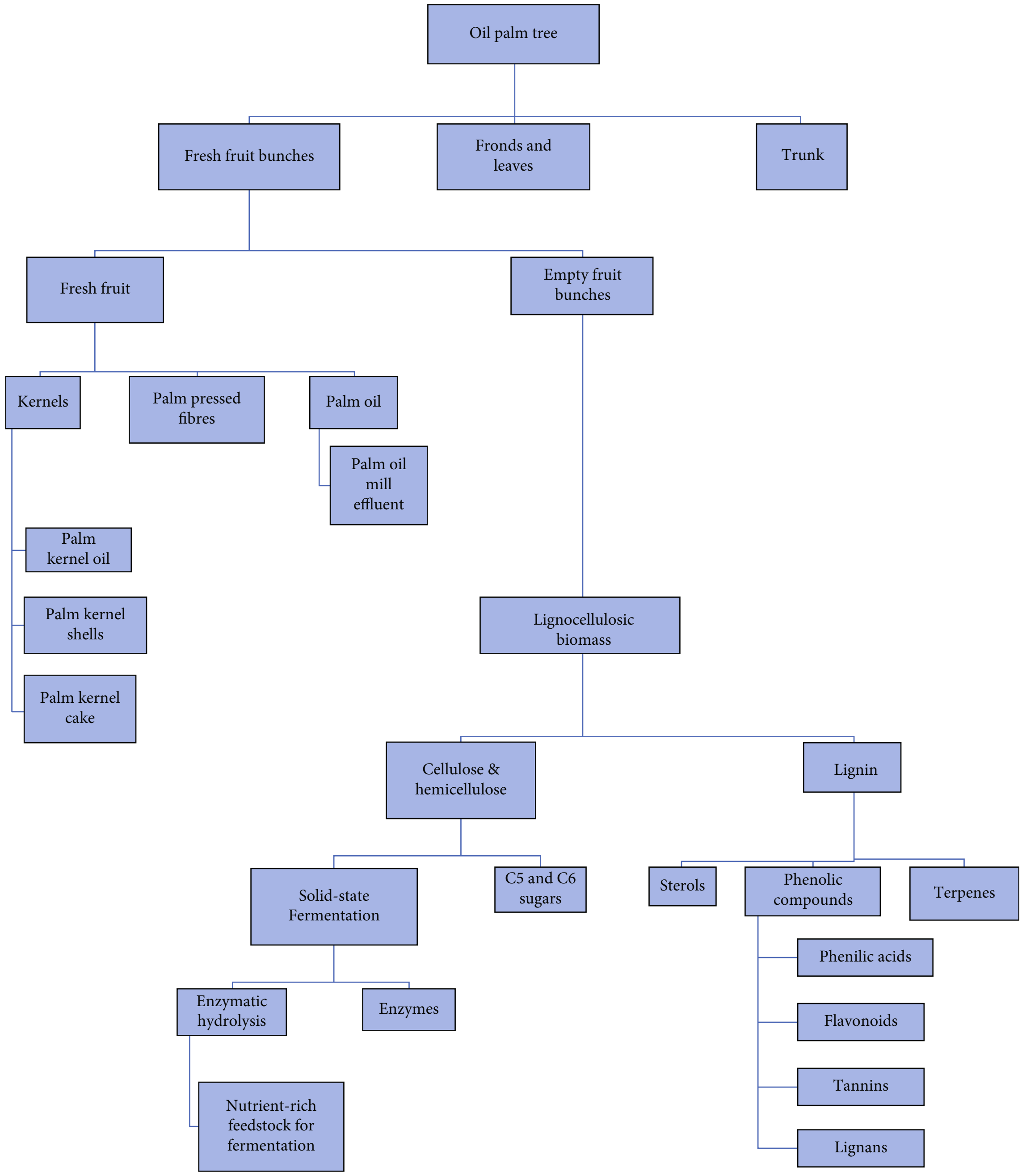

Figure 2: Oil palm tree parts and by-products [2, 3].

on the backbones of CNCs [10, 30]. Drug carriers are commonly spherical, as this shape is the simplest to manufacture [14]. Nevertheless, rod-shaped particles possess high body cellular absorption and a long circulation duration, making them effective as drug carriers and increasing the kinetics of blood clearance [6, 14]. Rod-shaped CNCs demonstrated a significant potential for drug delivery as they controlled active chemical releases and allowed the loading of charged and neutral drugs or medications, which could be transported to the selected areas owing to their negative surface charge, adsorption ability, and high specific surface area ratio [6, 11, 12].

The enhanced open pore structure, considerable surface area, superior bioavailability, and capabilities of CNC-based hydrogels to deliver a higher amount of therapeutic drugs have attracted much interest, particularly in the biomedical and pharmaceutical industries [13, 16]. The freeze-drying approach, which requires no additional treatment or solvent, is employed in producing CNC aerogel that aids the ability to load drugs and increases the bioavailability of drugs. The unbleached cellulose of OPEFB is used to create the CNC/CNF-mixed aerogel. The aerogels exhibit outstanding macroporous and lamellar structures due to the slow freezing step at 20°C before freeze-

Table 1: The summary of research conducted using OPF in the medical field ($n = 24$).

Focus	Field	Matrix or filler	References
Drug transportation	Pharmacology	The CNC and CNF from OPEFB	[8]
		The CNC from OPEFB	[9]
		Fibrillated CMF from OPEFB	[6, 7, 10–19]
Tissue engineering	Biomedical engineering	The OPEFB-derived CNC hydrogel	[5]
		The OPEFB cellulose	[7, 20–24]
Antimicrobial agent bearer	Microbiology	The CNC from OPEFB	[7, 14, 25, 26]
Wound care administration	Dermatology and internal medicine	The CNF from oil palm biomass	[27]
		The OPEFB-generated cellulose acetate	[28]

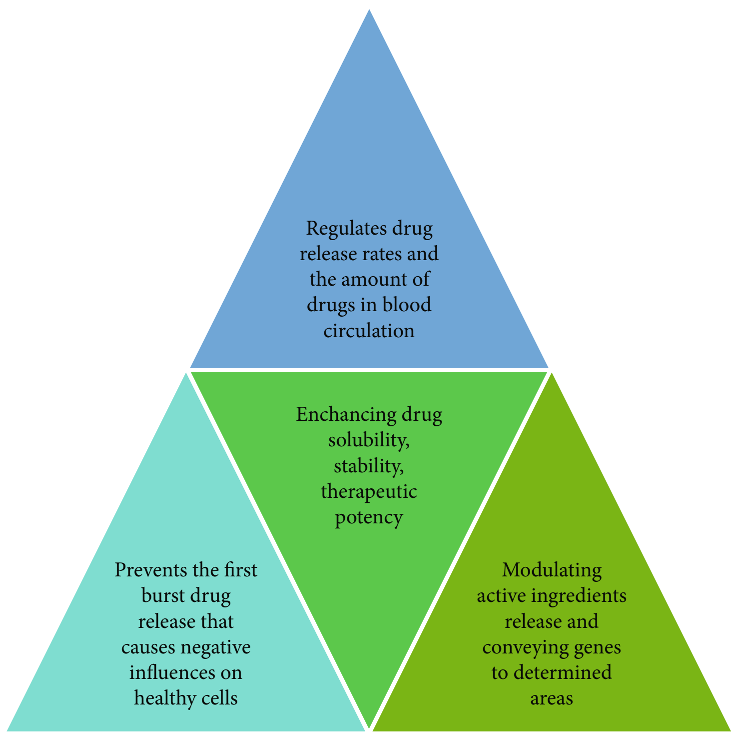

Figure 3: Uses of CNC in drug transportation.

drying, producing lightweight, highly porous, high crystallinity, and specific surface area products that could be employed in drug transportation [8].

Shazali et al. [9] generated spherical CNC from OPEFB with fluorescein isothiocyanate (FITC) to test cellular internalisation into normal murine fibroblast cells and rat glioma for potential anticancer drug nanocarrier use. The normal and malignant cell lines could not absorb the FITC-CNC well. The study reported that the C6 (rat glioma cells) and NIH3T3 (normal murine fibroblast cells) general adsorptive endocytosis controlled the surface characteristics, morphology, and hydrophobicity of the nanoparticles. Cell aggregation was further hampered by the electrostatic interaction between the negatively charged CNC surface and the fibroblast cell membrane obtained in the study. Therefore, the CNC could not attach to cell surfaces and initiate the membrane-wrapping step. Studies suggested altering surface charge properties to increase FITC-CNC cellular absorption into malignant cells to obtain a customised nanocarrier for transporting anticancer medications [6, 9].

A material extrusion technique employed to produce desired hydrogels for various applications with liquid-based materials is direct ink writing (DIW) three-dimensional (3D) printing. Cellulose nanofibrils are the primary material utilised in fibrillated cellulose printing as they naturally possess shear-thinning traits that allow smooth extrusion. At moderate shear rates, cellulose nanofibrils are highly viscous, enabling them to be 3D printed while still maintaining their shape. Furthermore, the fibrillated cellulose could adhere to the therapeutic agents and codrug carriers to the targets and control medication release (antibiotics and anticancer drugs). The attribute is critical to diminishing the adverse impacts of cytotoxic chemotherapy on nontargeted cells and tissues [17]. A high-speed homogenisation-manufactured fibrillated cellulose in DIW 3D printing has several advantages, including a large surface area, aspect ratio, and fibre entanglement that contributes superior mechanical features and could be utilised in the approach [17, 18].

Mohan et al. [17] isolated and fibrillated cellulose microfibres (CMF) from oil palm biomass to procure a sturdy and flexible cellulose-based 3D-printed composition with intact cellulose fibrils. They partially dissolved the CMFs in an alkaline solvent to obtain the desired product. They also documented that CMF-printed structures such as scaffolds and human ear cartilage produced considerable accuracy, shape fidelity, and better mechanical properties. They also tested calcium carbonate ($CaCO_3$) as the drug transporter in the 3D-printed CMF/$CaCO_3$ composite. The preserved fibrillated form of the CMFs obtained in the investigation recorded the ability to regulate the uptake and release of 5-fluorouracil (5-FU), a therapeutic medication. The CMF printable composite also exhibited potential for usage in applications involving regulated drug administrations and prevented the first burst drug release with adverse influences on healthy cells.

4.2. Tissue Engineering. Repairing damaged tissues, bones, and cartilage reconstruction and accelerating wound healing with minimal displeasure are the aims of tissue engineering technology [23]. Tissue engineering technology is also favoured for developing new therapies and repairing and rejuvenating harmed tissues and organs [7]. Consequently, CNC-based substances are highly desired in tissue engineering technology investigations as they fulfil conditions such as increased cell adherence and division, better mechanical properties, capacity to hold water, water permeability, biodegradability, and sustainable growth [7, 21]. The desired features of CNC-based substances in tissue engineering technology are as shown in Figure 4.

Some techniques involved during tissue engineering scaffold synthesis include electrospinning, solvent casting, freeze-drying, cross-linking, and 3D printing [20, 24]. Nevertheless, 3D printing is the only technique that reportedly employed OPF to procure tissue engineering. A 3D cross-linked hydrophilic polymer or hydrogel could absorb significant liquid or saline solution volumes. The material also exhibited capabilities for employment in tissue engineering due to its biocompatibility [5]. Athukoralalage et al. [23] documented using 3D bioprinting nanocellulose hydrogels for tissue engineering. The hydrogels in the report were successfully evaluated for mammalian cell viability and tissue engineering implementation. Furthermore, the research results demonstrated that the 3D-printed structures improved accuracy and resolution.

Salleh et al. [22] reported that OPF cellulose, which was dissolved in a sodium hydroxide (NaOH)/urea solvent and mixed with sodium carboxymethyl (NaCM), produced a superabsorbent hydrogel. This hydrogel was documented to exhibit maximum gel fraction, water absorption, degree of swelling, and transparency at 10% epichlorohydrin (ECH), which is utilisable in tissue engineering technology. Conversely, the assessment results (gel fraction, water absorption, and degree of swelling) were the lowest at 5% ECH, except for moisture retention. This was reported due to improved cross-linker concentration from high internal osmotic pressure, which boosted the superabsorbent characteristics of the hydrogel. The hydrogel's super-absorbent and water-holding abilities demonstrated significant potential for further employment in tissue engineering technology.

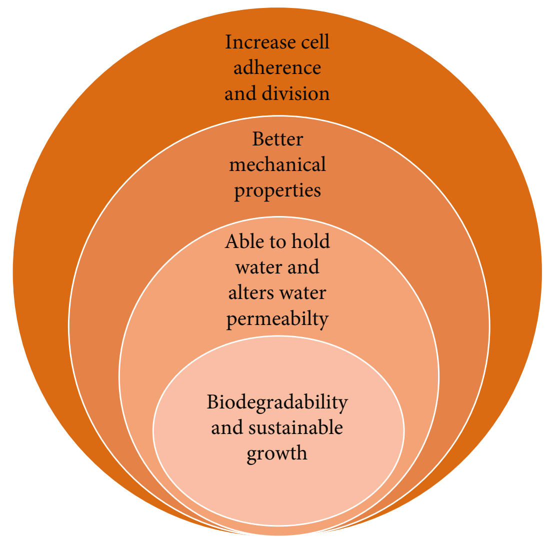

Figure 4: Characteristics of CNC-based substances that are highly desired in tissue engineering technology investigations.

4.3. Antimicrobial Agent Carrier. Due to resistance, antibiotics have been reported as less potent in treating infections. Microorganism mutations and selection pressure from antibiotic treatments allowed mutant strains a competitive edge, leading to a global spread. Selective pressure describes a naturally occurring selection in which one organism obtains benefits over another [25]. Some microbes are killed by particular antimicrobial agents, while some thrive, mutate, and proliferate over time, leading to more antimicrobial-resistant microbes [26]. Figure 5 shows the process of selective pressure affecting the resistance of microbes to antibiotics over the year.

Bacterial strains were detected long before the first penicillin antibiotic was introduced. Antibiotic usage has resulted in selection pressure, which has led to almost all disease-causing microorganisms developing antibiotic resistance towards the antibiotics employed to treat them [25]. The antibiotic resistance evolution due to microbial mutation and the reduced effectiveness of antibiotics in curing prevalent microbial diseases prompted the manufacture of novel antimicrobial carriers [25].

Adhering active antimicrobial agents to long-chain polysaccharides and polymers, primarily CNCs, which act as transporters, is becoming a common practice [7]. Curcumin ((1,7-bis (hydroxyl-3-methoxyphenyl)-1,6-heptane-3,5-dione), a fat-soluble compound with orange-yellow pigment, is obtained from turmeric (*Curcuma longa L.*) [32]. It is a naturally occurring polyphenol known for its exceptional pharmacological attributes, including anti-inflammatory, antioxidant, antibacterial, anticancer, and antimutagenic

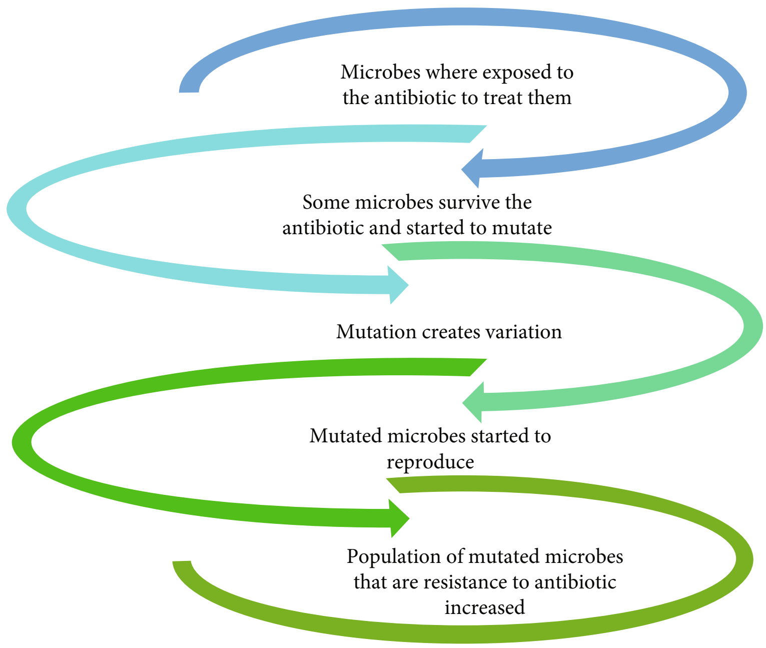

Figure 5: Process of selective pressure affecting antibiotic resistant [31].

Table 2: Summary of advantages and disadvantages of CNC scaffolds as reported by Suteris et al. [28].

Advantages	Disadvantages
1. High porosity responsible for absorbing excess wound exudation and preventing microbial infiltration	1. Scarring
2. Outstanding results in cell adhesion, multiplication, motility, and diversification	2. Wound constriction
3. Substantial surface area for drug loading and administration	3. Inadequate host cell/tissue integration
4. Oxygen permeability through the dressing	4. Limited due to the challenges associated with selecting reasonably priced and ecologically suitable solvents
5. Water vapour transfer to give sufficient moisture for wound healing	

[14, 32]. Curcumin was reported to have low toxicity in humans and animals [33]. In addition to its antimicrobial property, Foo et al. [14] effectively bonded curcumin (Cur) to OPEFB-derived CNC altered with tannic acid (TA) and decylamine (DA) to obtain a potent and superior green antimicrobial drug transporter. The adjusted CNC recorded curcumin-binding efficiencies within the 95–99% range for every measured concentration, at least twice that of the unmodified CNC. The extraordinary binding efficiency was similar to commercially available wood-based CNC.

4.4. Wound Care Application. Compared to conventional graft or allogenic skin tissue methods, wound dressings made of plant- and animal-based natural polymers, for example, cellulose, have recently received tremendous recognition in regenerative medicine. Cellulose possesses unique properties that can imitate the features of extracellular matrices (ECM), causing it to be appealing within all-natural polymers. The open market offers a variety of materials for wound dressings, including foams, hydrocolloids, hydrogels, and electrospun nanofibre scaffolds. Even between them, electrospun nanofibre scaffolds have unique benefits, several of which include high porosity responsible for absorbing excess wound exudation and preventing microbial infiltration, outstanding results in cell adhesion, multiplication, motility, and diversification, as well as a substantial surface area for drug loading and administration, oxygen permeability through the dressing, reaching the wound site, and water vapour transfer to give sufficient moisture for wound healing. Moreover, electrospun bioscaffolds have unique qualities, including solid biocompatibility, promotion of epithelisation, and adequate holes for gas exchange [28].

However, even with these promising benefits, some scaffolds have disadvantages, namely, scarring, wound constriction, and inadequate host cell/tissue integration. Three-dimensional (3D) scaffolds have gained recognition in this regard for their ability to cover wounds and establish a solid physiological defence against infection from the outside. Although cellulose has benefits as a wound healing medium, the availability of electrospun cellulose nanofibre scaffolds is limited due to the challenges associated with selecting reasonably priced and ecologically suitable solvents [28]. Table 2 summarises the advantages and disadvantages of CNC scaffolds.

Methicillin-resistant *Staphylococcus aureus* (MRSA) and other bacteria could impede wound healing and cause exudation. Zinc oxide (ZnO) has gained attention in nanofiller studies due to its high stability, exceptional photocatalytic performance, antibacterial activity, and nontoxicity [27]. Consequently, Supramaniam et al. [27] procured CNFs from oil palm biomass overloaded with zinc oxide (ZnO) nanocomposites for treating wounds. The ZnO-CNF samples recorded a 2 mm inhibitory zone in the MRSA antibacterial evaluation conducted during the investigation. The report also suggested that oil palm biomass-derived nanocellulose could be successfully utilised for various biological utilisations.

Suteris et al. [28] fabricated cellulose acetate (CA)/polycaprolactone (PCL)/Cur nanofibre scaffolds with EFB-generated cellulose acetate (CA) as the vital element for utilisation in wound dressing. The hydrogen bonds between the components resulted in improved hydrophilicity, which enhanced the swelling properties of the scaffolds. The article noted that the nanofibre scaffolds utilised in wound healing developed more significant multiplication and actin creation in fibroblasts than scaffolds without Cur. Furthermore, the cell growth observed in the study proved that the drug-loaded nanofibres were safe for the cells. The CA/PCL/Cur nanofibre scaffolds exhibited potential application as a material for drug conveyers in skin tissue engineering with good physical and biological capabilities for wound healing. Nevertheless, merely a few effective skin scaffolds have been found for tissue engineering employment despite extensive studies on producing the biomaterial.

As most of the studies reported the use of OPF in the form of CNC in multiple areas within medical potential, up to date, we could not find any article which reports a clinical trial regarding OPF or its derivative.

4.5. Future Prospects. With the latest developments in the medical engineering field, the use of nanocellulose from OPF can be further explored to increase its usage. The nature of nanocellulose that is capable of being a catalyst for medicinal substances allows it to function as an intermediary to further improve function and effectiveness, especially in medical engineering technology.

5. Conclusion

The OPF has wide applications and capabilities in the medical area, particularly in the biomedical and pharmaceutical sectors. It is utilised for drug delivery, tissue engineering, and wound dressing. The substance also exhibited promising results and significant capacities to be exploited and further researched. Nonetheless, hydrophobicity, poor drug-loading characteristics, accumulation, and phase detachment from matrixes during manufacture due to the high surface energy area are among the limitations of OPF that require solving. These restrictions necessitate further investigations to acquire solutions to optimise the potential of OPF.

Data Availability

Any data related to the study can be readily provided upon reasonable request.

Conflicts of Interest

The authors declare that there is no conflict of interest to be declared.

Authors' Contributions

Nurul Syafika Atikah Babu, Mohmed Isaqali Karobari, and Nor Aidaniza Abdul Muttlib provided substantial contributions to conceptualisation (lead), visualisation (lead), writing—original draft (lead), and writing—review and editing (supporting). Rabihah Alawi contributed to the writing—review and editing (lead).

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