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Encapsulation of bioactive agent (Curcumin, Moringa) in electrospun nanofibers – Some insights into recent research trends

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ABSTRACT

As the epidemic of coronavirus disease (COVID-19) has spread rapidly, health organizations around the world has made wearing face mask obligatory to prevent the spread of the infections for the wellness of the society. As wearing face masks become a daily routine, the usage of cloth facemasks from textile fabric, is popular among the public. Since antiquity, textiles have been proven to be intertwined with human lives and the integrant of these crucial materials are fibers. Particularly, nanofiber fabrics manufactured by electrospinning have attracted attention, owing to the better filtration efficiency and breathability. In addition, the electrospinning process provide opportunities to fine tuning of the surface functionality through polymer chemistry and an encapsulation of bioactive agents in single step process. This review opens up a new horizon in possible textile applications especially, an active layer of bioactive agent (Curcumin and Moringa) loaded nanofibrous fabrics-based facemasks for day to day life.

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1. Introduction

Approximately, it has been six months since Sars-CoV-2, caused the pandemic disease of COVID-19 and not all the countries in the worldwide have recovered from such pandemic situation. Amidst of these conditions, researchers have played a prominent role in investigating the materials and protective devices, that can be used for controlling the spread of coronavirus diseases. The exponentially increased the affected cases in china of COVID-19 diseases has observed by World Health Organization (WHO) and declared the global health emergency on 30th January 2020. To protect their own people, many countries have implemented the full or partial lockdown and some restrictions especially the border also closed between countries. An effective vaccine or treatment not yet introduced for COVID-19. However, the transmission of virus has suppressed by some preventing procedures like wear the face mask, maintaining social distance, practicing hand hygiene and so on, which has been remained an uncompromised routine to protect themselves, till date. In accordance with that, it is mandatory to wear face masks in public places such as transport, shopping, etc., especially when leaving the house [1–3].

As wearing face masks become a daily routine, the health organizations around the world encourage public to use cloth (textile fabric) face masks and not masks such as N 95 and surgical masks or those required by healthcare workers. In line with the above opinion, the researchers are engaged in fabricating three-layer face mask using non-woven nanofibers with superior properties over conventional fabric masks. While it should be agreed that wearing facemasks cause troubles for certain people, particularly those who have to hold them on during full workdays or with existing skin conditions [4].

Nowadays, several researchers are working on utilizing natural bioactive agents for several skin care applications. Bioactive agents are compounds found in plants and in certain foods such as fruits, vegetables, nuts, oils, and whole grains. Examples of bioactive compounds include lycopene, resveratrol, lignan, tannins, and indoles that are being studied to help cure cancer, coronary artery, and other diseases. Among the various bioactive agents, Moringa oleifera (MO) of monogeneric family, Moringaceae and Curcumin of ginger family, Curcuma longa L, remained popular among people looking for good skin heath [5,6]. Low saturated fatty acids and

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high amounts of olive oil present in the MO leaves, flowers, green beans, seeds and seed oil (Saini et al., 2016), are a great source of nutrients and vitamins [7]. In addition, the leaf of MO has antimicrobial, antioxidative, antifungal properties. Some studies, MO leaf extracts has been used to coat the textile fabrics in medical field [8,9]. Likewise, curcumin is a pigment which is existing in the turmeric, it has been used for centuries as a major food ingredient /additive and for skin care, owing to their anti-inflammatory, antifungal, antitumor activities, as well as a cancer chemopreventive agent [5,6].

There were several articles related to the outstanding properties of these natural bioactive agents infused nanofibers for wound healing and packaging applications [9–13]. However, there were no reports regarding their potential application in facemasks filter membrane using bioactive agent were provided. In this review, we summarized and offered possibilities for utilizing the nanofibers infused with these bioactive agents for facemasks application are discussed. In addition, this study focused particularly on *in vivo* and *in vitro* studies, rather than common comprehensive studies such as Attenuated Total Reflectance Fourier Transformed Infrared Spectroscopy (ATR-FTIR), Electron Microscopy (Scanning and Transmission), Structural (X - Ray Diffraction) analysis, mechanical and thermal properties.

2. Exclusive of electrospun nanofiber

Electrospinning is a realistic process consisting of spinning polymer solutions or melts that can easily be scaled up with high electric fields. With high electric fields that consist of spinning polymer solutions, electrospinning can be scaled up. A process schematic is shown in Fig. 1. The method is based on the idea that the weak surface tension forces in the charged polymer solution are overcome by strong electrical forces. To produce an electrically charged polymer solution jet that is expelled from the tip (Taylor cone) of a capillary tube and uniformly spread over the collection substrate, a high voltage is used. The jet then travels in the direction of the external electrical field and elongates according to the external and internal electrical fields. The jet is deposited on a substrate randomly which is like a nonwoven mat of nanofibers (Composite and hollow nanofibers). This technique only appropriate for polymeric solutions like Synthetic and natural polymers which have been treated into nanofibers with individual diameters ranging between few nanometers and several microns. The key benefits of the electrospinning method are the production of very thin fibres with wide surface areas to the order of a few nanometers, ease of functionalization for different applications like biomedical engineering, healthcare, environmental air filtration, water purification and so forth [10–14].

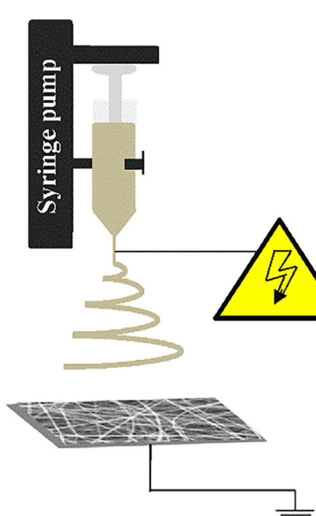

Fig. 1. Experimental set-up for electrospinning.

3. Bioactive agent (Curcumin (Cur) and moringa oleifera (MR)) loaded nanofibers

In general, among the numerous fabrication techniques, electrospinning process remains a simple way of achieving bioactive agent loaded nanofibrous scaffolds for biological applications.

Polat *et al* (2019) fabricated curcumin (Cur) loaded polyurethane (PU) blend fibers for wound dressing and investigated the effect of concentration of polymers and curcumin on morphology, diameter, and contact angle values of the nanofibers. In addition, it is also suggested that these kinds of bioactive agents are a good alternative against conventional chemical-based materials [15]. In yet another work, curcumin loaded with the blended polymers of poly ε–caprolactone/chitosan (PCL/CTS) nanoscale nonwoven fabric was fabricated via electrospinning process. The above prepared nanofibers were also analyzed via *in vitro* technique and suggested for wound healing process [16].

Mohammadi et al., (2019) infused anti-cancer drug chrysin and cur with PCL/Polyethylene glycol (PEG) nanofibers and performed *in vitro* drug release and *in vivo* wound-healing studies in male rats. The study found that in several stages of the wound healing process by affecting the Interleukin (IL-6), matrix metalloproteinases (MMP-2), tissue inhibitor of metalloproteinase (TIMP-1, TIMP-2) and inducible nitric oxide synthase (iNOS) gene expression and each gene expressions varied each other due to the varying of concentration of dose [17]. In another study, Yang et al (2019) studied the traditional Chinese herbal medicine of cur and Lithospermi radix (LR) extract and added within Gelatin-based nanofibrous membranes to advance wound healing in a streptozotocin (STZ)-induced diabetic rat model. *In vivo* animal wound healing assay exhibited higher recovery rate and outperformed the control groups in terms of collagen synthesis, TGF- production, anti-inflammatory effect, and promoted the wound healing process [18].

Furthermore, Wang et al. (2015) prepared the Cur-loaded polyvinyl pyrrolidone (Cur/PVP) nanofibers. The resultant of *in vitro* cytotoxicity assessment demonstrated that the cell viability for Cur (20 and 40 μg/ml) in PVP nanofiber was decreased to 24.4 and 20.9%. In vivo Pharmacokinetics (PK) test and anticancer treatment were examined on Naïvemale C57BL/6 mice, and observed that the mouse plasma increased to 167 ng/ml at 60 min. The Cur/PVP nanofiber demonstrated much higher efficiency in inhibiting tumour growth compared to both pure PVP and Cur for *in vivo* anticancer treatment. [19].

Akman et al (2019) studied the potential of nanofibers containing food-grade gliadin loaded with different amounts of curcumin were investigated. The increment of 2.25% of cur loaded gliadin nanofibers (CLGN) showed controlled release of cur and protected its free radical scavenging ability. Furthermore, the encapsulation of 2.25% of cur within nanofibers were enhanced the antioxidant and antibacterial activities (Staphylococcus aureus (*S. aureus*) and Escherichia coli (*E. coli*)). The resultant of these CLGN could be an available carrier for the delivery of cur and has the potential applications in the food industry and other bioactive delivery systems [20]. Li et al (2017) employed blend electrospinning process to fabricate cur-loaded mesoporous silica incorporated nanofiber mats and polyvinyl pyrrolidone (PVP) for hemostasis. The prepared fibrous mats were specially focusing on the hemostatic effects using *in vivo* and *in vitro* studies by injured animal liver model. The results showed that *in vitro* assessment of CCM-MSN (<8 wt

Table 1
Summarize the polymers used in bioactive agent with findings.

S.No.	Polymer material	Diameter of nanofiber (nm)	Findings	Refs.
1.	Polyethylene oxide/Hydroxypropyl methylcellulose/ Curcumin	138 ± 39	In vitro study of solubility test	[27]
2.	Chitosan /Polylactic Acid (PLA)/ Curcumin	66.81	Wound Healing and cytotoxicity	[28]
3.	Polycaprolactone/Gelatin/ Curcumin	123 ± 18% to 133 ± 20%	Antibacterial studies against *MRSA* and *Extended Spectrum Beta-Lactamase*	[29]
4.	Xanthan-Chitosan polysaccharides / Curcumin	760 ± 250	In vitro study against $Caco_2$ cell	[30]
5.	Gelatin / Curcumin	181 ± 66	For wound healing applications	[31]
6.	Poly vinyl Alcohol/ Moringa stenopetala seed protein	232 ± 59	Thermal stability up to 170℃ for water treatment	[32]

%) loaded PVP electrospun nanofibers had no evident toxic effect on the growth of L929 cells and antibacterial effects against *methicillin-resistant Staphylococcus aureus* (MRSA). It was highly recommended that cur-loaded mesoporous silica incorporated PVP nanofiber mats good biocompatibility and antibacterial activity [21]. Mamidi et al (2018) fabricated implantable cur embedded in blended polymer of gelatin/polylactic acid (GL/PLA/Cur) aligned nanofiber (diameter: 295 nm) scaffolds by forcespinning concentrations, for drug delivery and cancer therapy. Further, cell viability assay revealed that GL/PLA/Cur aligned fibers show excellent growth of human fibroblast cells and showed potential application in cancer therapy, drug delivery, and wound dressing [22].

For antimicrobial properties and wound dressing, Fayemi et al (2018) researched polyacrylonitrile (PAN) nanofibers with different concentrations of moringa leaf extracts. The antibacterial activity against *S. aureus* and *E. coli* was tested using the agar diffusion system and noticeable antibacterial activity was observed in the 15 mm inhibitory zone for *E. coli* and 12 mm in the inhibitory zone for *S. aureus* using the maximum concentration of PAN nanofibers filled with moringa leaves (0.5 g). Additionally, the wound dressing experiment was done with rat and the percentage of wound closure were also found with respective post-treatment time (1, 4, and 7 days). The resultant of wound closure percentage was higher (95%) in high (0.5%) loaded polymeric nanofiber [23]. In another study, the nanoencapsulation process of Moringa oleifera (1, 3 and 5%, w/w) extract within a biopolymer matrix of fish gelatine sourced gelatine matrix through electrospinning, was investigated by Hani et al (2017). CRL-1790 cells were used to reveal the in-vitro toxicological analysis and found the 95% cell variability was observed using the nanofiber mat (diameter 25 to 35 nm) at all applied MR extract concentrations [24].

Lin et al (2019) studied moringa oil contained chitosan nanoparticles (MO/CNPs) and MO/CNPs embedded gelatin nanofibers (3.0, 6.0, 9.0, 12.0 and 15.0 mg/mL) for biocontrol of *Listeria monocytogenes (L. monocytogenes)* and *S. aureus* on cheese. The bacterial species on cheese under 4 and 25 °C were evaluated for 10 days with negligible effect on surface color. It was observed that MO/CNPs nanofibers (diameter: 142.5 nm; surface thickness: 0.1 04 ± 0.003 to 0.124 ± 0.003 mm) wrapped on the cheese have revealed excellent antibacterial activity, thus demonstrating its potential for food packaging materials [25]. Zein polymer with Moringa Oleifera kernel oil-based nanofibers fabricated using coaxial electrospinning technique was studied by Owolabi et al (2019). The hydrophobicity of the obtained nanofiber diameter was 450 ± 24 nm and thermal studies were carried out for several applications in healthcare industries [26]. Additionally, Table 1 shows the various polymers are involved in bioactive agents for *in vitro* and *in vivo* studies.

4. Summary and outlook:

Wearing facemasks, maintaining social distance and following personal hygiene remained obligatory to avert the spread of the COVID-19 for the well-being of the society. However, wearing facemasks sometimes causes allergy and skin infections. In this short review, we had proposed an idea to infuse natural bioactive agents such as curcumin and moringa in the nanofibers of textile fabric. The proposed facemasks will be identified as anti-allergenic, anti-inflammatory and devoid of chemical odor. Associated with the individual effects of curcumin or moringa on the facemasks, the synergistic effects of curcumin and moringa will be expected to provide above said outstanding properties and retained the anti-viral performance for long duration.

The breathability and filterability of the nanofibers in the facemask are decided by the two conflicting morphological properties such as porosity and surface area of the fibers. Engineering the porosity and surface area to an optimum level via electrospinning technique opens a huge possibility of bio active agent loaded facemask. Electrospinning process with variations in technology such as coaxial or emulsion and forcespinning will provide cost – effective process with mass production capacity and possible morphological tuning of nanofibrous surface. By optimizing the collection time of the nanofibers, nozzle position and polymer/ bioactive agent concentration play a crucial role in determining the resultant nanofibrous surface as an active layer of the facemask fabric. It is suggested that the nanofibers with a dimension between 100 and 500 nm, arranged perpendicularly to each other forming a mesh like structure, will create better breathability while preventing pathogens to pass through [33]. In addition, the textile material with superhydrophobic nature will dry superfast, providing better fluid resistance. It is essential to make a note that the bioactive agent infused facemask should be made to adapt commercial standards, including breathability test (MIL-M-36954), fluid resistance test (ASTM F1862), particulate filtration test (ASTM F2299), bacterial filtration test (ASTM F2101), washable (ASTM F2100) and flammability test (ISO 4589 Part 2 standard). The present review highlighted the recent research related to curcumin and moringa. However, this concept can be extended to employing natural materials like lemon grass oil, neem and aloe vera.

CRediT authorship contribution statement

D. Sundhari: Writing - original draft, Conceptualization, Resources. **N.R. Dhineshbabu:** Conceptualization, Writing - original draft, Writing - review & editing. **S. Sutha:** Writing - original draft. **M.E. Raja Saravanan:** Supervision, Writing - original draft.

Declaration of Competing Interest

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

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