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A review of medicinal plant-based bioactive electrospun nano fibrous wound dressings

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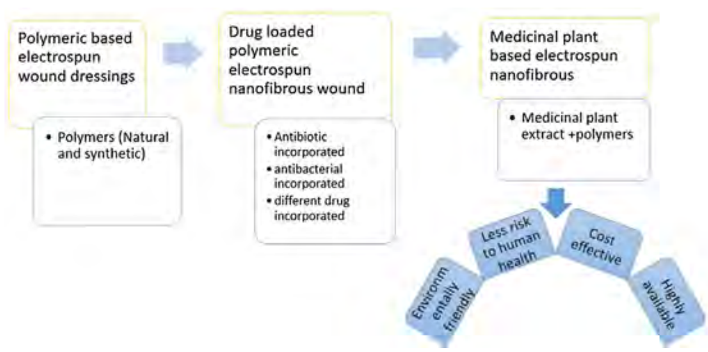
HIGHLIGHTS

- Medicinal plant incorporated electro spun nanofibrous wound dressings are latest research area.
- Developed medicinal plant based electrospun mats are none cytotoxic and biocompatible.
- They have no side effects, highly available, extracted easily environmentally friendly.
- A number of tradational medicinal plants are available in the world.

GRAPHICAL ABSTRACT



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ABSTRACT

In the early time, natural materials were used only to cover the wound but nowadays wound dressings contain functionalize materials to prevent infections, assist wound healing process, and improve skin restoration. Among dissimilar forms of wound dressings, electrospun nanofibrous wound dressings are the latest and promising ones due to their unique properties. These dressings have morphological similarity to the natural extracellular matrix (ECM), high surface area to volume ratio, greater porosity, continuous and flexible nano structure fibers applicable for drug delivery systems which can approve tissue regeneration, wound fliuid transportation and ensure breathability for cellular growth and proliferation. This review provides a broad overview of latest medicinal plant incorporated bioactive electrospun nanofibrous wound dressing researches and developments. It also discussed the therapeutic properties of different traditional medicinal plants.

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1. Introduction

The skin is the largest and outermost organ of the human body. It is a barrier between human body and the external environment, which has the function of maintaining temperature balance, preventing excessive fluid loss, and preventing pathogens from invasion Hongli Ye, Junwen Cheng [1,2]. Once the skin is damaged, there maybe fluid exudate in the injured area, this fluid with body temperature and nutritions there maybe development of infection in wounds which may bring illness of patients, even lead to passing away [3]. Different biomedical textile materials with different manufacturing techniques are used to cover and heal the wound. An ideal wound dressings must have basic characteristics as biocompatible, non-toxic, protective against infection, absorbable, permeable, and quick drug delivery [4-11]. Most wound dressings

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are based on textile constructions in the form of fibres, yarns, non-woven, woven, crochet, knitted and braided fabrics, composites and electrospun nanofibrous materials. Foams, films, hydrogels, matrix, and hydrocolloids are also used [8].

Among the above forms of wound dressings, electrospun nanofibrous mats are advanced and alternative due to numerous unique advantageous properties over others, such as its morphological similarity to ECM, high surface area to volume ratio, greater porosity, permeability to oxygen, continuous and flexible nano structure fibers applicable for drug delivery [5,12]. These structural features approve tissue regeneration, transport wound fluid and ensure breathability for cellular growth and proliferation. Multifunctional nanofibrous membranes can be developed by incorporating some antibacterial agent, antibiotics, anti-inflammatory and healing agents easily during the electro spinning process [5,8,13-17].

There are different classifications of electrospun nanofibrous wound dressings by different researchers. One of electrospun nanofibrous wound dressings classification is written by Ramazan.E (2019) as passive, interactive, advanced, and bioactive. Another classification was by Ambekar, R. S and B.Kandasubramanian (2019) as polymer nanofibrous, polymer blend nanofibrous, biological molecules embedded polymers nanofibrous, drug embedded polymer nanofibrous, and hybrid nanofibrous wound dressings.

Passive wound dressings have only physical and structural properties functioning as preserving sufficient amount of moisture in the wound and to keep tissue disturbance from mechanical and infectious agent. Interactive electrospun wound dressings can response to cell and limits the growth of bacteria in the wound area. Advanced dressings are electrospun dressings with drug loaded to cure infections of wound. Bioactive electrospun dressings have characters to cure all features of wound having acceptable amount of physico-chemical and mechanical characteristics giving wound protection, inspiration of healing progression and removing bacterial from wound [8].

In this review, recent medicinal plant based bioactive electrospun nanofibrous mat used for wound dressing are discussed. Materials and their properties used for electrospun nanofibrous wound dressings, basic requirements and properties of electro spun nanofibrous wound dressing are included. Medicinal plants, their properties, parts of the plants and developed medicinal plant based electrospun nanofibrous wound dressings are also studied in detail.

2. Polymer based electrospun nanofibrous wound dressings

Natural biopolymers such as polysaccharides (alginates, chitosan, chitin), proteins (collagen, gelatin, fibrin, keratin, silk fibroin) and proteoglycans have attracted and given more attention for wound dressings preparation due to their morphological similarity to human macromolecules, biodegradability, biocompatibility, haemostatic, and non-toxicity. On the other hand, natural biomaterial has limitations as they have poor mechanical properties. Hence, natural biomaterials need modification by blending with other materials or polymers [8,15,18].

Some synthetic polymers have properties of biocompatibility, biodegradability and active groups that can improve cellular uptake used for wound dressing. Some of synthetic polymers used for wound dressings by electrospinning and their properties are shown in Table 1. Polyvinyl alcohol (PVA) is synthetic polymer mostly used for electro spun nanofibrous wound dressings by electrospinning. Even if it can be electrospun alone and used as wound dressings, it has disadvantages such as inappropriate hydrophilicity. Since hydrophilicity is the major property needed by wound dressings, to bring this property, it is mostly blended with other hydrophilic such as PVA/chitosan/starch [19], PVA/gelatin/chondroitin sulphate [20], and PVA/gum tragacanth [21] electro spun nanofibrous scaffolds.

Today, anumber of novel textile wound dressings are developed by combing polymers (both synthetic and natural biopolymers), antimicrobial, antioxidant agents including tradational plant medicines with multifunctionality to prevent infections, and facilitate the wound healing [8,13].

3. Medicinal plant based bio active electrospun nanofibrous wound dressings

Infection of wound is the main problem that delay the wound healing process. To avoid the wound infections, researchers are producing electrospun nanofibers functionalize wound dressings with antimicrobial agents, such as nanoparticles, and antibiotics. Among the antibiotic and nanoparticles loaded electrospun nanofibrous wound dressings are chitosan/alginate/gentamicin [22], silica/PCL/gentamicin [23], chitosan/PVA/Tetracycline hydrochloride [24], Chitosan/PVA/cefadroxil monohydrate [25], Chitosan/PEO/Teicoplanin [26], sodium alginate micro particles/poly(lactic-co-glycolic acid)/ciprofloxacin[27], sodium alginate/PVA/Moxifloxacin hydrochloride [28], ALG/polyethylene oxide/Vancomycin [29], sericin/PVA/Tigecycline [30], polylactide/Doxycycline [31], polyvinylidene fluoride/Enrofloxacin [32], PCL/gelatin/ZnO/amoxicillin [33], PCL/gelatin/ciprofloxacin hydrochloride [34], and PVP/Iodine [71].

Currently, there are many medicinal plants extensively used in traditional wound treatment in different parts of the world. i.e. many plants have the potential to treat wounds. The plants' phytochemicals such as phenolic, terpenoids and alkaloids have antimicrobial actions (see Table2). Due to nanoparticles and manmade antibiotics loaded electrospun nanofibrous wound dressings are harmful effects on the environment, and human health, loading of natural antimicrobial compounds extracted from plants to nanofibrous mats are becoming the new research area with the advantage that these natural compounds have inherent medicinal properties, non-toxicor fewer side effects, environmentally sustainable, easily available and less cost [35]. The publication in the area of plant extract electrospun nanofibrous materials is low as compared all publications. The first plant extract loaded in to electrospinning was Curcuma longa Longa. plant. At the first time, Curcuma longa Longa plant extract loaded Ultra-fine cellulose acetate fiber mats were manufactured by electrospinning [36]. Table 2 shows different traditional wound healing plants in which their extracts were incorporated in to nanofibrous by Nano spinning technology. The table (Table 2) also shows their properties, parts of the plant used for wound treatment and their possible extraction methods.

Different medicinal plant extracts, essential oils, and pure active ingredients were incorporated in to polymeric nanofibrous to integrate the physical properties of the structure of nanofibers to the chemical and antibacterial properties of the plants by electrospinning to produce nanofibrous wound dressing (see Table 3).

3.1. Turmeric (Curcuma longa)

Turmeric (Curcuma longa) is a herb in Zingiberaceae family with curcumin (diferuloylmethane) (3–4%) as a main bioactive component [66,75,77]. Curcumin is poly-phenolic compound with properties such as cytotoxic activity, anti-oxidant, anti-cancer, angiogenic, nerve healing properties and anti-inflammatory activities with innate antimicrobial characteristic [5,7,66,75,76,78,93-95], highly biocompatible and biodegradable. The draw backs of curcumin is low bioavailability, low solubility in water and unsta-

Table 1
Favorable candidate polymers used for wound dressings.

S. No.	Polymer	Polymer properties, advantages	Drawbacks	References
1	Collagen	Biocompatible, biodegradable, and non-toxicity	Fast biodegradable, low mechanical properties	[3]
2	Gelatin	Film formability, high tensile strength, hydrophilic, non-toxic air-permeability, biocompatible, wound healing, and homeostatic	Poor mechanical strength, higher degradation rat, low ductility	[1,19,25,26]
3	Silk Fibroin	Biocompatible, slow degradation, low immunogenicity, absorbable, permeable, easily processed into nanofibers, drug delivery carrier	Low molecular weight has poor mechanical properties	[9,24,25,27-31]
4	Keratin	Biocompatibility; capability of supporting cellular attachment	relatively low molecular weight and Pure keratin has poor mechanical properties	[32]
5	Chitosan	Biocompatible, biodegradable, antibiotic, antioxidant, wound healing capacity and decreased scar formation.	Not electrospun directly, limited solubility in organic solvents, lack structural stability in aqueous environments due to swelling	[1,16,21-24,31,33-41]
6	Alginate	Soluble in water & absorbable, excellent hemostatic agent, wound healing, non-toxic, biodegradable, biocompatible, drug control	rigid and fragile &lacks film formation ability	[42]
7	Hyaluronic acid	Biodegradable, biocompatible, visco-elastic and mucoadhesive properties, stimulation, proliferation and migration of fibroblast and keratinocyte tissues, modulating the inflammatory responses, reduce scare formation	High viscosity and surface tension, causes improper chain entanglement and electrospinning inability	[43]
8	PLGA	Drug delivery systems, gene transfer, favorable cytocompatibility and biodegradable, good biocompatibility	hydrophobic	[19,44,45,62]
9	Starch	Biocompatibility, biodegradability, non-toxicity, similarity to native cellular matrix and wound-healing property	Poor mechanical properties	[46]
10	PVA	Biocompatible, hydrophilic, biodegradable, water-soluble, fiber formable, chemical resistance, non-toxic, and oxygen permeable	inadequate elasticity, &lacks required hydrophilicity, poor stability in water	[13,19,20,47-50,65,67]
11	PCL	Biodegradable,biocompatable, high mechanical properties, and stable polymer in ambient condtions	slow degradation rate, poor hydrophilicity	[5,17,19,51-54,58,69]
12	PVP	Biocompatible, non-toxic, soluble in alcohol/water, absorbable		[55]

Table 2
Traditional wound healing plants used for Electrospun Nanofibrous.

S. No	Medicinal plant	Plant part	Extraction method	Properties helping for wound	Reference
1	Azadirachta Indica	Leave	Methanol	antibacterial, antioxidant, anti-inflammatory	[103-105]
2	Turmeric		microwave, ultrasound and enzyme-assisted	Biodegradable, anti-oxidant, angiogenic, anti-inflammatory, antimicrobial	[5,7,49,93,95,97]
3	Clerodendrum phlomidis	Leave	n-hexane, ethyl acetate, ethanol, methanol	anti-inflammatory, hepato protective, anti-hypertension, anti-oxidant properties	[106]
4	Gymnema sylvestre	Leave	Ultrasound, Cold maceration assisted	anti-microbial, wound healing, anti-inflammatory	[80]
5	Carica papaya	Leave	ethanol, water chloroform	hydrophilicity, antimicrobial, healing	[26]
6	Aloe vera	Leave	Water	antidiabetic, and anti-inflammatory	[3,53,100]
7	Lawsonia inermis	Leave	Ethanol, water	wound healing, antibacterial activities	[87,95,101,102]
8	Garcinia mangostana	Fruit	Acetone	antioxidant, antimicrobial, anti-proliferative, anti-inflammatory	[34]
9	Mucilage	Seed	Water	antioxidant, anti-inflammatory, promote cell growth	[86]
10	Clove	Flower	Water	antimicrobial, analgesic, antioxidant, anti-inflammatory	[33]
11	Zataria multiflora	Leave	Water	antibacterial, antifungal, anti-inflammatory	[12]
12	Pomegranate	Fruit	Methanol	wound healing	[88]
13	Achillea lycaonica		Ethanol-water	antioxidant, antimicrobial, antispasmodic, healing, and anti-inflammatory	[44]
14	Corn			anti-oxidative, anti-microbial, supports cell adhesion, proliferation	[105]
15	Fenugreek	Seed		antioxidant, healing	[90]
16	Lamiaceae family		ethanol, limonene and ethyl lactate, pressurized liquid	anti-bacterial, anti-inflammatory, anti-nociceptive	[109]
17	Chamomile			antibacterial, healing	[51]

ble to alkaline, thermal treatment and light which limits its applications alone and it requires different carriers, like cyclodextrins, to be used in therapeutic use [70,75,78].

Curcumin Longa is the first medicinal plant loaded on electrospinning. At the first time, Curcuma longa Longa plant extract loaded Ultra-fine cellulose acetate fiber mats were manufactured by electrospinning from cellulose acetate solution of 17% w/v in 2:1 v/v acetone/dimethylacetamide and curcumin in various amounts (i.e., 5–20 wt% based on the weight of CA powder). A potential curcumin based bio medical nanofibrous wound dressings were manufactured such as polyvinyl alcohol/curcumin[75], polyvinyl alcohol/cyclodextrins/curcumin[78] by electrospinning without changing the chemical structure of curcumin during the electrospinning. Curcumin was also loaded in to poly (ε caprolactone)/gum tragacanth nanofibers to produce scaffolds for diabetic wounds resulting an increase in collagen content and promote healing in the early stages, released curcumin for about 20 days, and have property of antibacterial against Staphylococcus aureus [5]. Shahid, M.A., et al.[66] developed polyvinyl alcohol/honey/-turmeric extract nanofibrous through electrospinning, the nanofibers enhanced moisture management properties, and antibacterial activity.

A novel three-layer poly e-polycaprolactone/polyvinyl alcohol/curcumin nanofibrous was developed by electrospinning technique. Anti-bacterial tests showed that 16% curcumin fibrous exhibited anti-bacterial activity without sacrificing the acceptable

Table 3
Developed medicinal plant based electrospun nanofibrous wound dressings.

S. N.	Electrospun nanofibrous wound dressings	Properties investigated	Reference
1	Chitosan/PEO/semelil (herbal extract drug)	high swelling, release of semelil	[39]
2	Chitosan/PVA/gelatin/Zataria multiflora	Non-toxic and biocompatible, antibacterial property	[12]
3	Cellulose acetate/gelatin/Zataria multiflora	Wound healing, antibacterial property	[87]
4	Vitamin E/starch nanoparticle/silk fibroin/PVA-aloe Vera	Biocompatible, non-toxic, release vitamin E, protect cells from toxic oxidation products	[98]
5	Polyurethane/cellulose acetate/graphene oxide/silver/curcumin	Biocompatible, antibacterial property, promote wound healing rate	[108]
6	PVA/curcumin	Biocompatible, non-toxic, anti-bacterial, release of curcumin	[93]
7	PVA/honey/Curcumin	Good moisture properties, antibacterial activity	[49]
8	PCL/gum tragacanth/curcumin	Fast wound closure, collagen deposition, regenerate epithelial layer, healing, release curcumin, antibacterial	[5]
9	PCL/PVA/curcumin	Absorbable, anti-bacterial property, biocompatible	[53]
10	Thiocarbohydrazide modified gelatin/curcumin	Non-toxic, antibacterial, release curcumin	[96]
11	PVA/Schizophyllan(mushroom extracted)	improved cell adhesion, wound healing, cell proliferation and migration and have good swelling property	[109]
12	PVA/gelatin/Carica papaya	Antibacterial, hemocompatible, non-toxic, wound healing	[26]
13	PVA/mucilage	promote cell growth and fibroblasts cells attachment, biocompatible, anti-inflammatory	[86]
14	PLA/achillea lycaonica	Non-toxic, compatible, release of achillea	[44]
15	PCL/clerodendrum phlomid	Superior mechanical property, wettable, anti - bacterial and antioxidant activity, releasing capabilities of Clerodendrum phlomid	[106]
16	PCL/gelatin/lawsone	wound re-epithelialization, antibacterial, biocompatible, healing	[87]
17	PCL/gum arabic/Corn protein	Biodegradable, porosity, antibacterial, good mechanical properties	[105]
18	PVA/chitosan/Azadirachta indica (neem extract)	Antimicrobial property, biodegradable, absorbable, porous	[103]
19	Silk fibroin/Fenugreek(natural antioxidant)	Biocompatible, wound healing, antioxidant property	[90]
20	Silk fibroin/collagen/fenugreek	Biocompatible, wound healing, antioxidant property	[110]
21	Silk fibroin/soy protein isolate	Biocompatible, biodegradable, non-toxic, wound healing activity	[89]
22	PCL/Gymnema sylvestre leave extract	Biocompatible, antibacterial, mechanical property, wettability	[80]
23	Polyvinyl pyrrolidone containing isatis root	excellent wetting, permeable, antibacterial activity, wound closure	[101]
24	PCL/PVA/Chitosan/Eugenol	biocompatible, non-toxic, antibacterial action, release Eugenol	[47]
25	Cellulose acetate/Thymol/β-cyclodextrin	Non-toxic, drug release, antibacterial activity	[107]
26	Polycaprolactone/Thymol/tyrosol	Bactericidal and anti-inflammatory property	[100]
27	Silk fibroin-PCL/silk fibroin-hayluric acid-thymol	Biocompatible, wound healing, antioxidant and antibacterial property	[100]
28	Chitosan/PVA/honey/Nepeta dschuparensis	Biocompatible, biodegradable, faster wound healing,tissue regeneration	[92]

level of cell viability. Poly e-polycaprolactone guaranteed desirable mechanical properties and non-adherence feature to the wound, and polyvinyl alcohol used for absorption of exudates [70].

To avoid the toxicity and additional burst release of curcumin, Kulkarni, A.S., et al.[94] produced non-toxic curcumin/thiocarbohydrazide modified gelatin nanofibrous mat for wound healing applications, 50% acetic acid as solvent which avoids the use of toxic fluorinated solvents, and then cross-linked using N-(3-dimethylami nopropyl)-N'-ethylenecarbodiimide hydrochloride). In the mat curcumin was articulated as amorphous nano solid dispersion. The result revealed that the higher crosslinking percentage is the higher hydrophobicity of fiber mat and the lower release rate. 1% curcumin in the nanofibrous mat exhibited optimum slow and steady release at neutral pH which could favour the effective release of curcumin at the wound site and also displayed enhanced mechanical strength along with effective no inhibition compared to 2 and 3% curcumin.

Shahid, M.A., et al.[66] manufactured honey combined with turmeric extract by ethyl acetate and loaded polyvinyl alcohol by electrospinning and produced antibacterial nanofibrous mat with better moisture management properties compared to polyvinyl alcohol electrospun nanofibrous mat alone.

Generally, researchers tried to work that turmeric extract successfully loaded to different biopolymers to have the wound dressing antibacterial properties. Also researchers worked on controlling of turmeric from nanofibrous by adding some complex molecules such as cyclodextrins.

3.2. Aloe vera

Aloe Vera is a plant known for its traditional medicine for treating burn wounds. It has many various biological properties like antidiabetic, anti-inflammatory, and wound healing properties due to its ability to stimulate fibroblasts and enhance the healing process such as collagen synthesis and maturation [3,81,96]. It constitutes of amino acids, vitamins, sugars, minerals, and enzymes that support general healthiness. Even if aloe vera lacks electrospinnability and appropriate mechanical characteristics [70], it can be incorporated in to nanofibrous mats.

Hybrid biocomposite gelatin/aloe vera-PCL nanofibrous scaffold was manufactured through double nozzle co-electrospinning by grlatin/Aloe vera and PCL solutions from two different syringes. The scaffold showed an optimum uniform size distribution, low diameter, ideal biological properties and appropriate mechanical characteristics using 10% and 7.3% concentrations of gelatin, and aloe Vera respectively. It was found that the incorporation of Aloe vera enhanced fibroblast proliferation compared to PCL and Gelatin-PCL, scaffold. In addition, the fabricated scaffold presented appropriate drug delivery, biodegradability and antibacterial activity and may be used for skin tissue engineering applications [97]. Also Kheradvar, S.A., et al.[98] produced core-sheath nanofibrous mat of silk fibroin/poly(vinyl alcohol)/aloe Vera as a new vitamin E (VE) delivery system by electrospinning.

3.3. Lawsonia inermis

Lawsonia inermis also called henna is used as a medicinal plant due to it contains phenolic compound. The leave of henna extract has antibacterial activities anthelmintic, immunomodulatory, antitumor, antioxidant, UV protective, wound healing and antimicrobial properties [82-85], but lawsone has weak solubility in aqueous as a result do not achieve its maximum pharmaceutical activity. Encapsulation of lawsone is one means of increasing its solubility, stability, sustained release and bioavailability [82]. Adeli-Sardou, M., et al.[82] encapsulated lawsone in to PCL/gelatin polymers in the core–shell architecture to produce PCL/Gelatin/lawsone nanofibrous mats by coaxial electrospinning, PCL in the outer shell polymer and gelatin-lawsone blend in the inner core. The scaffolds have released lawsone for 20 days and 1% of lawsone loaded mat ensured the highest healing by increasing re-epithelialization of wound after 14 days and has excellent characteristics which can be used as wound dressing as a medicine.

A solution of Lawsonia inermis also incorporated into gelatin and poly-L-lactic acid to produce poly-L-lactic acid/Gelatin/Lawsonia inermis hybrid nanofibrous scaffolds [83]. The nanofibrous scaffolds can release Lawsonia inermis, have antibacterial properties against Escherichia coli and Staphylococcus aureus which could prevent wound infection and accelerate wound healing. Avci, H., R. Monticello, and R. Kotek [84] similarly incorporated Lawsonia inermis leave extracts (2.793 wt%) in to PEO and PVA to produce nanofibrous scaffolds by electrospinning, resulting bactericidal properties against Staphylococcus aureus and bacteriostatic action to Escherichia coli.

Also bioactive gelatin-oxidized starch/Lawsonia Inermis aqueous extract nanofibers were developed for treating second-degree burn wounds [99]. Nanofibers are continuous, smooth, and bead-free fibers in 70/30 ratio of gelatin-starch. The result reveals that as Lawsonia Inermis content increases, fiber dimeter reduced and the addition of Lawsonia Inermis improved fibroblasts attachment, proliferation, collagen secretion, and antibacterial activity, and accelerated wound closure in vivo studies and reduced the inflammatory response and macrophage numbers.

3.4. Azadirachta Indica/Neem

Azadirachta indica is traditional medicinal plant exhibiting a wide spectrum of biological activities such as antibacterial, antifungal, antiviral, antioxidant, and anti-inflammatory properties. It contains a number of bioactive constituents, azadirachtin as main constituents [72-74].

Azadirachta Indica can be incorporated in to electrospinning solutions of polymers to manufacture active nanofibrous wound dressings. [72], methanol extracted azadirachta indica leave was incorporated in to polyvinyl alcohol/chitosan solution and electrospun in to nanofibrous using bi-layered system. Since chitosan is brittleness it is difficult to collect after electrospinning, the PVA solution alone was electrospun as background and then chitosan/neem/PVA solution was electrospun. The mat was smooth, degradable, porous with 91% porosity, homogeneous images and having the minimum and maximum diameter of 152 nm and 298 nm respectively. The neem addition improved thermal stability, absorbability, synergistic antibacterial action against Staphylococcus aureus bacteria through the formation of inhibition zone [72].

3.5. Zataria multiflora

Thymus, Ocimum, Origanum, Monarda genera, Zataria multiflora and Nepeta dschuparensis Bornm are in the family of Lamiaceae flowering plants. All parts of Zataria multiflora plants are aromatic which have a phenolic compound called Thymol (2-isopropyl-5-methylphenol) found in thyme essential oil, as a main component. Thymol is an effective natural antibacterial component, anti-inflammatory, anti-nociceptive, cicatrizing and antimicrobial properties [91,100].

Thymol restricted to be used in biomedical areas because of its low water solubility, poor bioavailability, and high volatility. Chen, Y., et al. [91] tried to form a water soluble inclusion complex of Thymol and β-cyclodextrin and then incorporated into cellulose acetate fibrous matrix via electrospinning. The result revealed that fibrous film showed continued drug release, long-lasting antibacterial activity against S. Aureus, porous structure and good cytocompatibility which could be an attractive candidate for wound dressing material. Miguel, S.P., et al. [100] also produced Thymol based wound dressings of two layerd nanofibrous scaffolds, silk fibroin/poly(caprolactone) as top layer to act as a physical barrier at the wound site, silk fibroin/ hyaluronic acid/Thymol as the bottom layer to enhance the wound healing process and to prevent wound infections.

Ardekani, N.T., et al [12] incorporated zataria multiflora essential oil into chitosan/poly(vinyl alcohol)/gelatin solutions to electrospun in to nanofiber mat wound dressing. The nanofiber mat containing 10% of zataria multiflora essential oil was non-toxic, biocompatible, inhibited growth of Staphylococcus aureus, Pseudomonas aeruginosa, and Candida albicans. The mat has high swelling property which promising alternatives to conventional wound dressings. Farahani, H., et al.[87] also manufactured zataria multiflora based cellulose acetate/gelatin/Zataria multiflora nanofibrous mat wound dressing.

3.6. Nepeta dschuparensis Bornm

Nepeta dschuparensis Bornm is widely used as a traditional herbal medicine due to antibacterial, antioxidant and anti-inflammatory properties as it contains flavonoids, essential oil, β-caryophyllene, 1.8 cineole, thujone, β- eudesmol and pinene [92]. Naeimi, A., et al. [92] designed and fabricated Polyvinyl alcohol/Chitosan/Nepeta dschuparensis bornm/Honey bio-nanofibrous scaffold for burn treatment using electrospinning and investigated as wound healing property.

3.7. Chamomile plant

Chamomile is one of the Asteraceae family and a common medicinal plant which contains different effective substances such as phenolics and flavonoids apigenin, quercetin, patuletin, luteolin, and their glucosides. Apigenin is the most abundant quantitatively in chamomile flower showing a notable effect on wound healing process [68]. Chamomile extract can be incorporated in electrospinning solutions, [68] electrospun chamomile extract with poly (e-caprolactone)/polystyrene blend to produce non-toxic(in vitro study) active nanofibrous mat wound dressings, in a mixture of chloroform/DMF (7/3) as a solvent, to accelerate the wound healing in vivo (15% chamomile extract) and have anti-bacterial and anti-fungal activities as compared to poly(e-caprolactone)/polystyrene nanofibers. Chamomile addition decreases the fiber diameters.

3.8. Isatis root

Isatis Root is a well-known traditional medicine used to treat infectious diseases including skin diseases as a result of its good antibacterial and anti-inflammatory activity. Hand held electrospinning of PVP/isatis root fibers was produced for wound healing purpose. 10 wt% isatis in the nanofibrous mat gave air permeability sufficient to permit gaseous exchange, good surface wettability and antibacterial activity against common gram positive and gram negative bacteria and more rapid wound healing [101].

3.9. Fenugreek

Fenugreek, belong to Leguminosae family, is the oldest medicinal plant used in treating wounds and other diseases with potential antioxidant properties which could increase wound healing. studied feasibility of fenugreek (natural antioxidant) use in nanofiber production by preparing novel electrospun scaffold wound dressing from fenugreek and silk by co-electrospinning method and treated with ethanol vapour (75% ethanol vapour) to improve stability in water and to bring structural changes from silk I (random coil) to silk II (β sheet). The fenugreek incorporation to silk nanofiber scaffold exhibited high biocompatibility, antioxidant and wound healing and collagen deposition in vivo study. It also showed superior mechanical, thermal and optimum porosity [90].

3.10. Melilotus officinalis

Melilotus officinalis is an herbal used for wound treatment. Semelil is herbal drug extracted from Melilotus officinalis for managing diabetic foot ulcers. Mirzaei, E., et al. [56] incorporated Semelil extract from Melilotus officinalis in to chitosan/polyethylene oxide and produced nanofibrous through electrospinning. The fibrous have a releasing capabilities of the drug and can accelerate wound-healing.

3.11. Achillea lycaonica

Achillea lycaonica plant is in a species of Achillea, most of these species have biological activities of antioxidant, antimicrobial, antispasmodic, wound healing, cytotoxic activities and anti-inflammatory and used in medicinal areas. 1:1 ethanol–water extract show the best antioxidant property. Achillea lycaonica plant extract was mixed with pure poly (lactic acid) and fabricated in to nanofibrous mats. The mat showed excellent cell compatibility and increased the viability of cells, no cytotoxic effect, can release Achillea lycanica. The mat also has appropriate tensile strength which promise potential for cell proliferation activity that cause faster and better wound healing. Achillea lycaonica plant extract in the mat reduced the diameter size of electrospun nanofiber which could be attributed to the increase in electrical conductivity [61].

3.12. Corn

Corn has a protein, 80% of the protein is called Zein protein. Zein protein is non-toxic, biodegradable, flexible and high thermal resistance and biologically active which has anti-oxidative, antimicrobial properties, supports cell adhesion, proliferation and penetration that is used as a potential medical application. Corn protein can be electrospun with polymers for wound dressings. Zein protein was mixed with polycaprolactone and gum arabic to produce a novel polycaprolactone/Zein/gum Arabic porous nanofiber scaffold by electrospinning. Zein and gum arabic can give antibacterial property and polycaprolactone polymer for elasticity, strength and time setting of scaffold degradability, and tensile strength desirable for skin tissue engineering [89].

3.13. Pomegranate

Pomegranate is a small tree or shrub which contains significant amounts of polyphenolic compounds such as ellagic acid, ellagic tannins, flavanols, anthocyanins, catechin, procyanidins and gallic acid. The tree contains pomegranate peel in the fruit, of 50% the pomegranate fruit weight, that have higher amounts of polyphenolic compounds than pomegranate juice and possess stronger biological activity with promising wound healing potential. Pomegranate peel can be extracted by methanol extraction method. Pomegranate extract was mixed with Manuka honey, bee venom (a colourless, acidic liquid excreted by bees) and polyvinyl alcohol to fabricate nanofibrous wound dressing exhibiting antibacterial activity against S. aureus and E. coli compared to negative controls, no cytotoxicity, and wound healing property [88].

3.14. Mucilage plant

Mucilage seed extract have biological properties of antibacterial, antioxidant, anti-inflammatory and promoter of cell growth and traditionally used as treatment for skin and other diseases. Aqueous mucilage extract was mixed with aqueous PVA solution to electrospun in to nanofibrous mat, PVA (10% w/V) as an aiding agent for electrospinnability. By the addition of mucilage, the nanofibrous improve its biocompatibility and cell adhesion and growth [86].

3.15. Cloves plant

The clove tree has flower buds containing a natural phenolic component called Eugenol, an essential oil extracted from cloves. Eugenol has therapeutic properties of antimicrobial, analgesic, antioxidant, anti-inflammatory which will improve healing process for wound. But, Eugenol has disadvantage of poor water solubility and un-stability in the presence of chemical and enzymatic degradation, and will losses by volatilization or thermal decomposition [47].

Incorporating hydrophilic and hydrophobic bioactive agents in emulsion electrospinning prevents the loss of natural bio active agent's structural integrity and bioactivity. Mouro, C., M. Simões, and I.C. Gouveia [47] developed novel electrospun mats from polycaprolactone/polyvinyl alcohol/chitosan loaded with Eugenol extracted from clove tree, using chloroform/DMF solvent for polycaprolactone, water for polyvinyl alcohol and acetic acid for chitosan . The final mat showed rapid release of EUG during the first 8 h and increasing gradually up to 120 h, antibacterial activity against S. aureus and P. aeruginosa and cytotoxic in vitro study, biocompatibility. This showed the suitability of using Eugenol in to PCL/PVA/ CS as a potential new innovative wound dressing to prevent and treat microbial wound infections.

3.16. Mangosteen (Garcinia mangostana linn

Garcinia mangostana is a tropical fruit used as medicine traditionally to treatment wound infection and other diseases. Garcinia mangostana contains xanthone, α-, β- and γ- mangostins, garcinone E, 8-deoxygartanin, and gartanin. Extracts of garcinia mangostana show antioxidant, antimicrobial, antiproliferative, anti-inflammatory properties [51]. Therefore, extracts of garcinia mangostana can be incorporated in to nanofibrous polymers to enhance its antimicrobial and antioxidant properties.

[51] prepare Chitosan-ethylenediaminetetraacetic acid/polyvinyl alcohol (CS-EDTA/PVA) nanofiber mats and incorporated acetate extracts of fruit hull garcinia mangostana (1, 2 and 3% wt α-mangostin) to enhance antibacterial and antioxidant efficiency of the mat for enhancing wound healing. The result revealed that the mat exhibited anti-oxidative, antibacterial activity, can release the extract and stability. And also has wound healing in vivo and the mats provide appropriate tensile strength and swelling properties.

3.17. Clerodendrum phlomidis

Clerodendrum phlomidis is a species of flowering plant in the family Lamiaceae have anti-inflammatory, hepato protective, anti-hypertension, and anti-oxidant properties used as folk medicine to control skin. Phytochemically, it has bioactive compounds of flavonoids, sterols, flavones, triterpenes, steroids, phenolic, glycosides and chalcone. Clerodendrum phlomidis leaf extract loaded PCL nanofibers by electrospinning technique was developed with superior mechanical properties, wettability, anti - bacterial and antioxidant activity, and good drug releasing property, promising to be used in wound dressing [79].

3.18. Gymnema sylvestre

Gymnema sylvestre is a herbal medicinal plant for wound treatment because of the following properties: anti-microbial, wound healing, anti-inflammatory. Its phytoconstituents include gymnemic acids, gymnemasaponins, anthraquinones, flavones, phytin, lupeol, and stigmasterol [80].

Ramalingam, R., et al [80] manufactured Gymnema sylvestre leave extract functionalized electrospun poly-ε-caprolactone nanofibrous wound dressing by electrospinning system. The result showed that the mat has properties of high biocompatibility, non-cytotox, antibacterial activity of Gram-positive and Gramnegative bacteria, superior mechanical properties, and wettability.

3.19. Carica papaya

Carica papaya is an evergreen shrub or small tree widely utilized for treating various diseases including skin diseases. The aqueous leave extract can accelerate progress healing of wound, antimicrobial activity, reduces odour, and hydrophilicity. Carica papaya riches in vitamin C (ascorbic acid) that acts as a co-factor for the proline and lysine hydroxylases that stabilize the tertiary structure of the collagen molecule, and facilitates the expression of genes responsible for collagen formation. The nanofibers of Carica papaya alone and loaded with some polymers is hydrophilic in nature allowing re-epithelization and wound healing process. A novel Carica papaya loaded PVA/Gelatin nanofibrous scaffold was manufactured by electrospinning for potential wound healing, with strong antibacterial activity against S. aureus and E. coli bacteria, no cytotoxicity against fibroblast cells, hemocompatible [39].

4. Conclusions

Day-by-day there are new understandings and discoveries of textile wound dressings. Consequently, researching and developing new functional wound dressings is still an area of research to meet the requirements of complex and un-healing wounds. Electrospun nanofibrous materials have special morphologies, high surface area to volume ratio and porous structure, haemostasis, capability of absorbing exudates, used as drug carriers, and capability to accelerate wound healing. Both natural and synthetic polymers can be used for electrospun nanofibrous material manufacturing, but combination of different polymers (synthetic and natural) will bring special properties for wound healing.

In recent wound dressings, bioactive ingredients of antimicrobials, antibiotics drugs, anti-inflammatory agents, traditional medicines are incorporated into the electro spinning solutions to produce new bioactive electro spun nanomaterials, that might be released to the wound to enhance wound healing rate and to have antimicrobial properties to reduce infections. It can be strongly argued that natural polymers and natural bioactive ingredients are leading in electrospun nanofibrous wound dressings, with numerous properties and advantages such as biocompatible, high swelling, non-toxic, antimicrobial and cost-effective as revealed from the researchers. As seen from the researchers Turmeric (Curcuma longa) or curcumin extracted from turmeric is the most widely used for active nanofibrous production for wound application.

Generally, we believe that electrospun wound dressings based on medicinal plants instead of metal nanoparticles and synthetic antibiotic drugs to impart antibacterial or other desirable properties are increasing because of no side effects, availability of medicinal plants, easily extraction, plant extracts have no or less side effects and environmentally friendly. These lead a promising possibility for clinical application useful in wound applications in the near future. But it can be concluded that there is no research done concerning the comfort-related properties and limited in their mechanical studies of electro Nano spun fibrous mats.

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CRediT authorship contribution statement

Biruk Fentahun Adamu: Conceptualization, Methodology, Investigation, Writing - original draft, Formal analysis, Investigation. **Jing Gao:** Conceptualization, Writing - review & editing. **Abdul Khalique Jhatial:** Writing - review & editing. **Degu Melaku Kumelachew:** Writing - review & editing.

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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