Ferulic Acid Polymers In Healthcare Applications

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ABSTRACT

Ferulic acid polymers, have importance in healthcare applications due to multifunctional groups derivatives of the ferulic acids act as an antioxidant, against ultra violate radiation damage, and are used in the treatment of many other illnesses. The review mainly focuses on important applications of ferulic acid in drug delivery, wound healing, antioxidant, and the role of ferulic acid polymer to cure those diseases. Due to reliable properties, ferulic acids and it polymers are found alternative and useful components of drug delivery in many important diseases with no toxic effect with less cytotoxicity.

Keywords— *Ferulic acid polymers; drug delivery; antioxidant*; and wound healing.

I. INTRODUCTION

Naturally occurring compounds have considerable interest in biological applications, due to their easy availability and less adverse effect on a healthcare application. Due to its easy availability and multiple derivatives of ferulic acid polymer, it has shown a variety of applications in health care, including wound healingantioxidants, easy drug release, and others.Poly ferulic acid with high molecular weight shows biocompatibility and degradable properties thus poly ferulic acid becomes a useful compound for drug delivery applications [1-3]. Unpaired electrons present in free radicals cause damage to certain organs like DNA enzymes and lead to dangerous diseases like diabetes, cancer, autoimmune and neurodegenerative disorders [1]. Along with this free radicals are undergoes chain reactions, for many diseases, and accelerate oxidative strength, atherosclerosis may lead to the death of patients. The single molecules of ferulic acid have various biological activities and the ability to react to stop free radical growth, thus here we thought to review the importance of ferulic acid polymers in healthcare applications [1]. In wound healing proliferation and repairing of tissue take place, collagen is found in the extracellular matrix and it is a useful component in the wound healing mechanism, ferulic acid, and its polymers act as a natural component for the enhancement of collagen production in the body in wound healing [10].To increase the solubility and stability of ferulic acid polymers and boost their cellular uptake, one strategy uses nanotechnology-based delivery systems, such as lipid-based nanoparticles, polymeric nanoparticles, or solid lipid nanoparticles. The ferulic acid polymers can be shielded against deterioration by these nanocarrier systems, which can also increase their bioavailability and allow for targeted distribution to particular tissues or cells[11].

II. APPLICATION OF FERULICACID POLYMERS

A. **Tuberculosis drug delivery**

Mariappan Rajana and co-workers'ferulic acid co-polymer synthesized by ring-opening polymerization and usefully shown application towards Tuberculosis drug delivery. TB is one of the most dangerous diseases caused by Mycobacterium tuberculosis. Rifampicin (RF), inhibit DNA-dependent polymerize and acts as an antitubercular agent.The author has reportedco-polymerization of Chitosan-on (ε-caprolactone) for the synthesis of CS-g-PCL viaring-opening polymerization in the microwave wave assistant method. Further grafting of ferulic acid was performed by using a coupling agent, at PH 7.4 in 1M acetic acid and 1M NaOH at a temperature of 45^{o} C. So, now they prepared 'CS-g-PCL/FA' Fig.1.The graftedcopolymerwas further converted to nano micelle and rifampicin was incorporated in the inner shell by ultrasonication [2]. Multiple functional groups such as carboxylic acids and hydroxy and methyl ether, allowed to do the modification of the main structure of ferulic acid, by which the properties can improved.

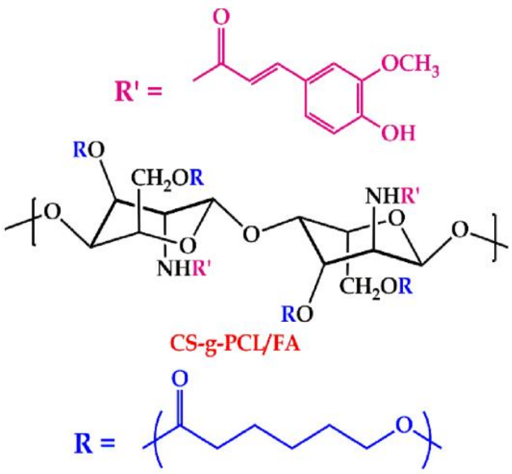


Figure 1: Chitosan-graft-poly(caprolactone)/(ferulic acid) polymer[2]

B. **Wound healing applications**

In disease diabetics Meletus due to the production of free radicals, wound healing has become a major problem. Claudia Carbone and a co-worker recently reported nanostructure lipid carriers of ferulic acid and Essential oil. A combination of ferulic acid and essential oil at homogeneous and with a small size of 150 mn, nano-stability, effects on cytocompatibility, and promotes cell proliferation and migration [3]. Due to FA's antioxidant and antidiabetic properties, a nano-particle of Polylactic acid grafted on poly ferulic acid was found useful in diabetic wound healing. Brahmeshwar Mishra and co-workers reported Ferulic acid- poly (lactic-co-glycolic acid) (FA-PLGA) nanoparticles preparation using nanoprecipitation methods, followed by characterization using SEM and TEM. The average size of the nanoparticle was 240 nm.

Nanoprecipitation method:

Poly (lactic-co-glycolic acid) was dissolved in acetone and drug material was added to this solution. Poloxamer 188 was dissolved in water. Thus organic phase containing polymer solution was injected into an aqueous solution through the syringe after 30 min. suspension was filtered through a 0.45μm membrane to remove excess stabilizer. The nonmaterial was converted to gel, by using Carbopol 980 molecules. For that purpose, the nonmaterial was added to Carbopol 980 aqueous solution, and the suspension was stirred to gel swell [3].

C. **Antiviral**

Ferulic acid naturally occurring phenolic acid and have two different functional groups on the aromatic ring. Thus, FA has multiple applications including antioxidant antiviral, and inhibitory action even if it shows applications in the food, agriculture, and cosmetic industries also. The best source of ferulic acid is crop waste such as wheat bran, rice bran, etc. Ferulic acid is a versatile building block for various bio-polymers. In the year 2013, Kathryn E. Uhrich et.al reported the ferulic acid biodegradable polymer with biological application and non-toxicity of polymer degradation. Aromatic hydroxyl carboxylic acids are mainly useful to develop biocompatible or biodegradable polymers. Developing such types of polymer material is a more difficult process thus, polymerization takes a long time to build up.In a recent discovery, Raghuraman et al. sulfated lignin in the sulfate group of Heparan sulfate was found active against the viral activity, author synthesized 4-hydroxy cinnamaldehyde-based carboxylate lignin by enzymatic oxidative coupling. And tested in cellular assays of herpes simplex virus-1 (HSV-1) infection compare to sulfated lignin carboxylate lignin where they found carboxylate lignin was found to inhibit HSV-1 entry into mammalian cells (IC_{50} = 8−56 nM). Lignin is an organic complex biopolymer,the conditional part of lignin is phenylpropanoid with a hydroxyl group. Carboxylic acid lignin CD and FD obtained, peroxidase catalyzed oxidative coupling of caffeic and ferulic acid both at the basic PH =8 in the dark. Naturally occurring phenol has various specific biological activities including antiviral, hepatoprotective, and vasodilatory actions. Vikas Pruthi and co-workers (4b) incorporated agro-waste Ferulic acid in bio-copolymer. The Natural ferulic acid was encapsulated in the electro-spun nanofibrous matrix of poly (D, L-lactide-co-glycolide)/polyethylene oxide. The author isolated ferulic acid from the Parthenium hysterophorus plant.

Electrospinning process:

PLGA:PEO:1:1 in DCM/DMF solution. A solution blend of this polymer with 2% of ferulic acid was prepared. The nanofiber of this blend was prepared by an electrospinning process with applied voltage (18 kV) and solution flow rate (0.5 mL/h). The characterization of nanofiber was done by using various spectroscopic techniques such as IR, DSC, and NMR, based on NMR study's author observed the shifting in chemical shift value of Ferulic acid encapsulated PLGA/PEO nanofibers.In the cytotoxicity of ferulic acid encapsulated PLGA/PEO nanofibers without ferulic acid does not show any cell growth while inhibition in cell growth is 71.3% in the case of nanofiber monitor in ferulic acid and ferulic acid encapsulated nanofiber. Thus the cytotoxicity of ferulic acid nanofiber shown in Fig.2

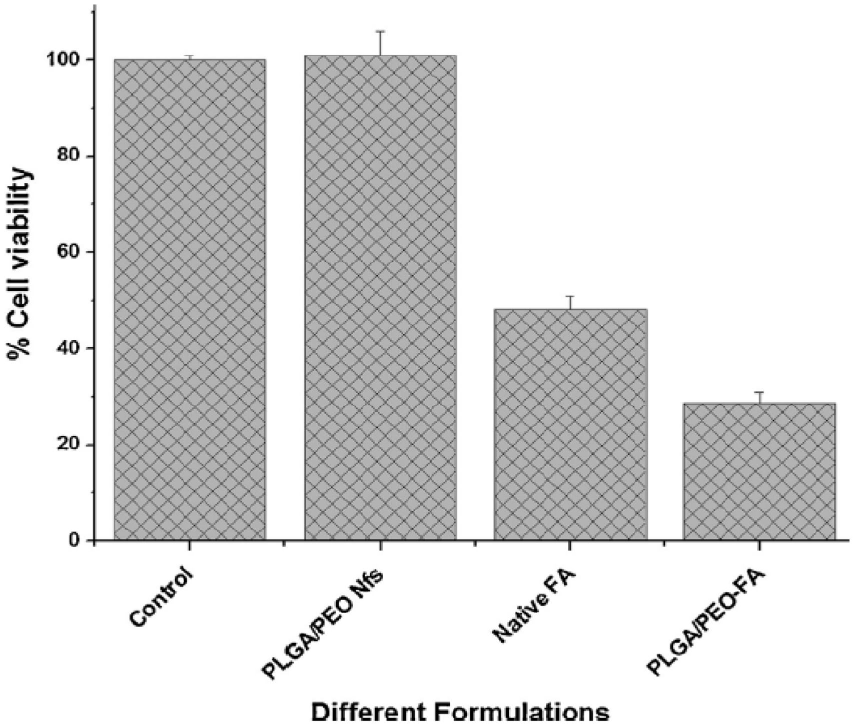


Figure 2: Showing cytotoxicity of different material studies [4b]

The average diameter for ferulic acid encapsulated PLGA/PEO nanofibers was recorded as 150 to 79.0 nm, and free radical scavenger activity of the nano-fiber was disclosed by using di(phenyl)-(2,4,6-trinitrophenol)iminoazanium (DPPH) assay [4b].[1]

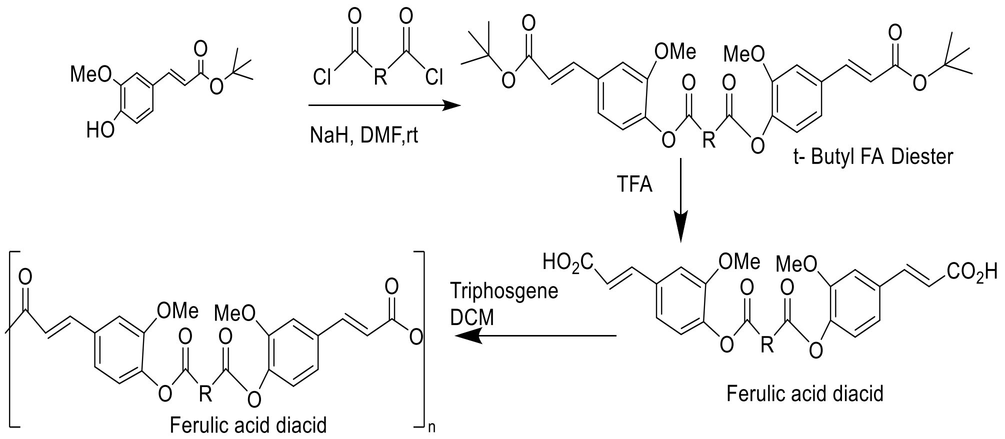
D. **Antioxidant**

Reactive oxygen species is essential for wound control and infection release for certain angiogenesis and cells. During a wound cellular damage take place and thus, in this case, antioxidant use for the removal of ROS, by which it can interactwith wound healing. Removal of ROS done by using polyphenolic acids. Liu and co-workers reported functionality (methoxy hydroxy group) on polyphenols on aromatic ring unaffected affect the anti-oxidant properties. The author found thatmodification of carboxylic acid with isocyanide found improvement in the antioxidant properties. Uncontrol blood loss isthe symptom, fortrauma lead to death in hospitals due to microbial infection in trauma would cause death in patients [5]. Free radicals are found as pathogens for many diseases including cancer, aging, and atherosclerosis. Formulation and incorporation of antioxidantswere found very difficult for the treatment of infectiousdisease.. in the year 2017(Prabhas V. Moghe and co-workers), a ferulic acid polymer as an antioxidant, in the treatment of inflammatory diseases, to atherosclerosis. The potential of degradable ferulic acid-based polymer nanoparticles to control macrophage foam cell formation by significantly reducing ox LDL uptake through the downregulation of scavenger receptors,The diseases of atherosclerosis is due to the oxidation of lipoprotein which results in foam cell formation the phenolic polymers due to antioxidant properties useful in the treatment of atherosclerosis. The amphiphilic micro polymer as a nanoparticle with antioxidant properties has been developed, author reported polyhydride ester ferulic acids nanoparticles to use as lipoprotein antioxidants [6].

E. **Drug delivery application**

Due to biocompatibility, ferulic acid is used in various biological activities including, anti-inflammatory, anticancer, antidiabetic, and pro-angiogenic applications. Purna Sai Korrapati and Balan Poornima reported Citosan-Polycarbonate nano-fiber was used for wound dressing and drug delivery applications.

Latex polymers have numerous varieties and various applications for industries. Latex polymers have multiple shapes in their morphological structure. Core-shell particle is one type of morphology which use for the preparation of latex with various essential properties. It can be composed of a minimum of two polymers, this type of core latex shell has applications in drug delivery, control release, and nanostructured material for electrochemical applications. Sylvain Caillol and co-workers develop two-stage emulsion polymerization of 4-acetoxy-3-methoxy styrene (AC4VG) and n-butyl acrylate for the synthesis of biobased core-shell particles. Solution co-polymerization of AC4VG styrene and *n*-butyl acrylate was carried out in toluene under an N_2environment and AIBN as initiators [7]. Ouimet and co-workers' reported poly-ferulic acid (anhydride ester) synthesized by reaction of the corresponding acid chloride with ferulic acid ester compound upon hydrolysis obtained carboxylic acid with linked with ester linkage that was used for drug release application (scheme 1) [8].



Scheme 1: Synthesis of dimeric ferulic acid polymer linking via linker

It was necessary to improve solubility to increase the efficiency of the ferulic acids polymers, author use FA-loaded polymer nanoparticles in drug delivery. Polymers polylactic acid and polylactic-co-glycolic acid were used to prevent the cytotoxicity of drug carriers. To verify the absence of cytotoxicity of blank carriers, a preliminary in vitro assay was performed on retinal pericytes and endothelial cells. FA-loaded NPs were subjected to purification studies and the physical-chemical properties were analyzed by photon correlation spectroscopy[9].

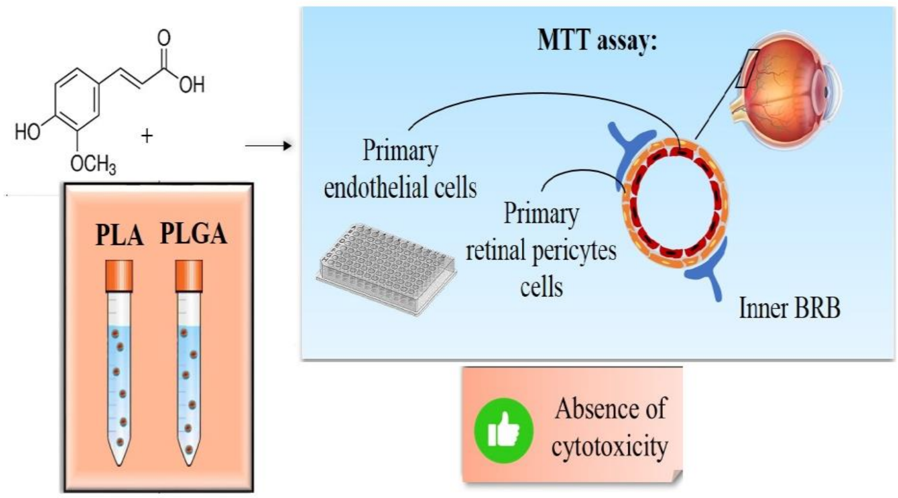


Figure 3: PLA and PLGA with ferulic acid for drug delivery

III. CONCLUSION

Ferulic acid polymers and ferulic acid composites are best for healthcare applications. It is also helpful in drug delivery applications due to its biodegradability and less cytotoxicity in high molecular weight also. Drug delivery and its effect on drug release in the presence of ferulic acid have been described in this chapter. Ferulic acid due to antioxidant and other important biological applications ferulic acid polymers are applicable such as wound healing anti-viral, cytotoxicity, and in the treatment of Tuberculosis.

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