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Biocompatible Gelatin Nanofibers as Potential Anticancer Drug Delivery Systems

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ABSTRACT

Abstract: Today, cancer remains a worldwide and severe public health challenge. Cancer is one of the reasons of disease and mortality global; chiefly owing to problems in treatment-associated, recurrence rates, metastasis and late diagnosis. In latest years, with the development of nano-materials, the investigation of drug delivery systems has become a novel field of cancer therapy. Local drug delivery systems are hopeful apparatuses in modern medicine because they can promise the release of drugs with the kinetics necessary; via specific applications and a reduction in unwanted side effects. Drug delivery systems are typically composed of delivery carriers, antitumor drugs, and even target molecules. Over the years, a wide variation of polymeric nano-mats has been explored as implantable single drug delivery systems. Gelatin is a natural polymer with highly biocompatibility and non-toxicity that is manufactured via thermal denaturalization of collagen, which is available in animal skin and bones in the presence of dilute acids. On the other hand, electrospinning is a widely considered method for the progress of drug-delivery nano-mats. 3-D Gelatin electrospun nanofibers (with great porosity and small pore size) can be applied to deliver anti-cancer drugs (like Doxorubicin, Tamoxifen and Curcumin) in cancer therapy. This mini review presents the gelatin nanofibrous anti-cancer drug delivery carriers for clinical application of cancer nanomedicine in the future.

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Introduction

Cancer is described as a wild growth of abnormal cells. It is assessed that there are more than 200 different kinds of cancer, usually named consistent with the tissue wherever the cancer was recognized for the first time. Now, the conservative therapeutic methods for the treatment of cancer are surgery, radiotherapy, and chemotherapy. On the other hand, nanotechnology has been actively combined as drug carriers over the past few years to treat several cancers (1-3). The main objective of nanomedicine in the treatment of oncological illnesses is to selectively carry the drug just to cancer cells. Up to now, numerous anticancer drugs like doxorubicin (DOX), curcumin (CUR), paclitaxel (PTX) and camptothecin (CPT) have been used in drug delivery structures (4).

Gelatin: A Biocompatible macromolecule

Gelatin is a biopolymer that is manufactured via thermal denaturalization of collagen, which is available in animal skin and bones in the presence of dilute acids. Gelatin contains of a great amount of glycine, proline, and 4-hydroxy proline residues (Figure 1) (5). Gelatin is extensively used biopolymer in several industries owing to its outstanding biocompatibility and biodegradability properties (6). Gelatin is a product of collagen hydrolysis, and is a natural, macromolecule that is considered as an perfect biomaterial used to biotechnology applications (7). In the next paragraphs, the various studies and researches based on *Gelatin nano-mats* in cancer treatment field will be highlighted and stated in detail.

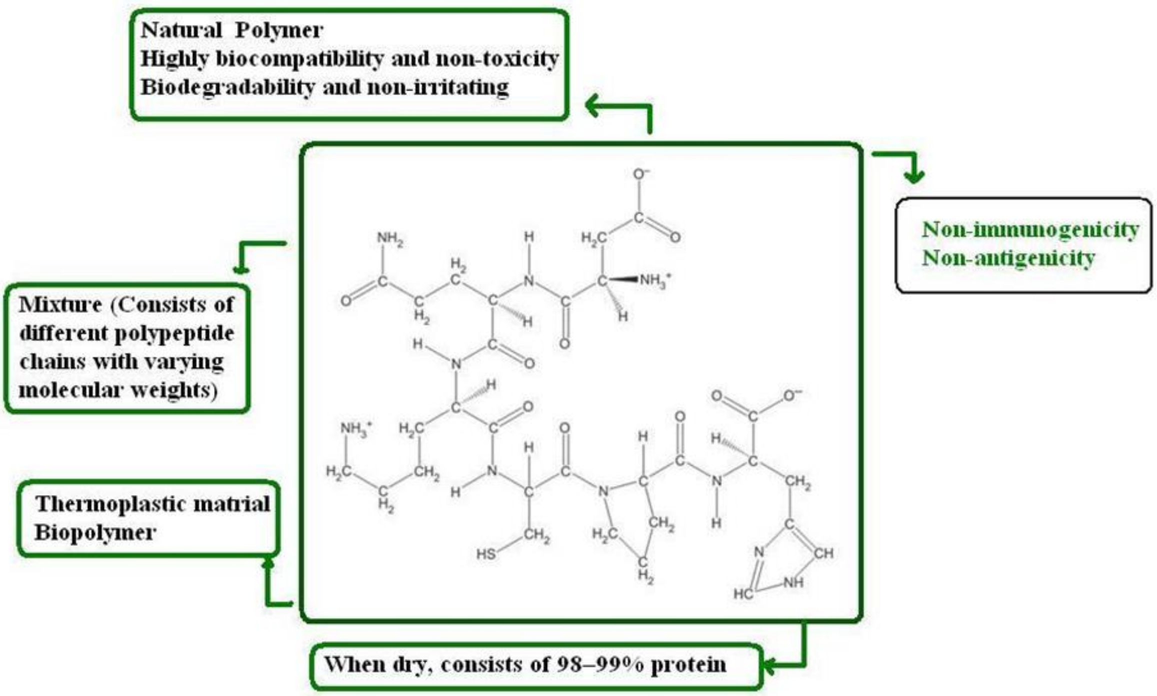

Figure 1. Gelatin. A natural polymer

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Electro-spun Gelatin Nano-mats

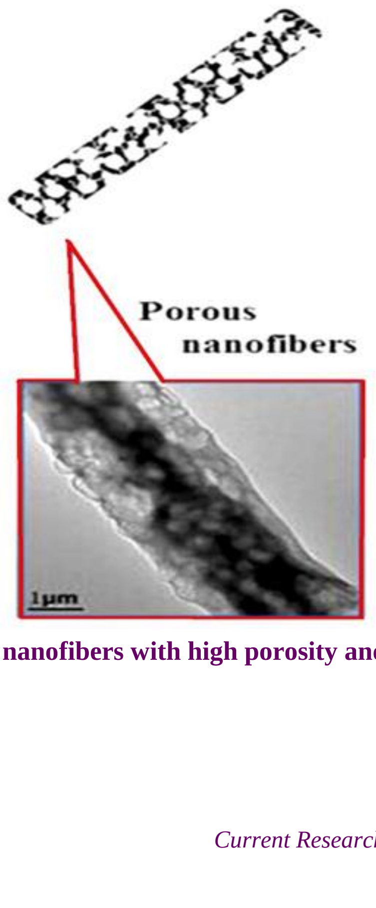
Nano-fibrous meshes refer to the structures made of ultra-fine polymeric fibers (8-10). The diameter of such fibers varieties from several micrometers down to few nano-meters, therefore are mentioned among nanotechnology and micron size world (11, 12). Such very small diameter results in a relatively high surface area to volume ratio (Approximately 100 m^2/g for a 100 nm diameter nano-fibrous mat) (13, 14). Such increase in surface area can significantly affect the physio-chemical and morphological properties of the nanofibers (15, 16).

➢ High porosity and small pore size

The technique that nanofibers are synthesized allow self-assembled nanofibers to align themselves into a characteristic 3D pattern, such as a honey comb meshes (17-19). Because of the small fiber diameter and high surface area to volume ratio, tiny pores in the range of 0.5 nm are formed within the nanofiber mesh, resulting in highly porous 3D structure (Scheme 1) (20, 21). Numerous synthetic, semisynthetic and natural polymers have been utilized to produce nanofibers (22, 23). Electrospun nanofibers offer several necessary structures as drug delivery systems (25,26).

1. The electro-spinning procedure can be used to manufacture nano-fibers from an extensive variety of solutions of both natural Polymers (27-29).
2. Nanofibers have high surface-layer area to volume ratios which provide efficient delivery of both hydrophilic and hydrophobic drug molecules (30, 31).
3. The drug release profile can be tuned to meet the specific clinical usage by modulating a variety of parameters, for instance the drug to polymer ratio, fiber diameter, morphology, and-or porosity (32-34).

Electro-spinning of gelatin delivers a hopeful approach to integrate the great presentations of gelatin with the perfect morphology and structure of electrospun nanofibers (35). As a water-soluble polymer, water is used as a solvent to dissolve gelatin for electrospinning use (36, 37).



Scheme 1. Electrospun nanofibers with high porosity and small pore size (24)

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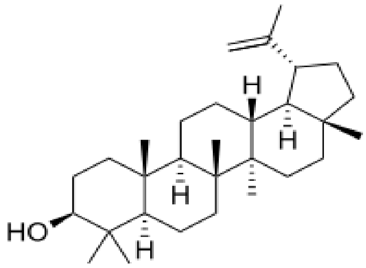
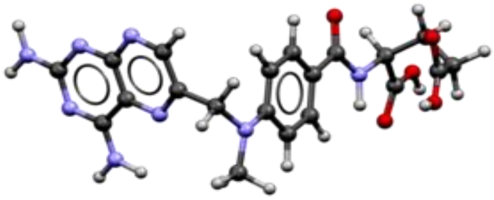
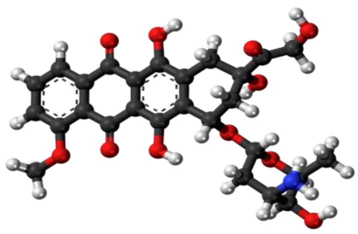
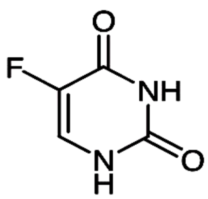
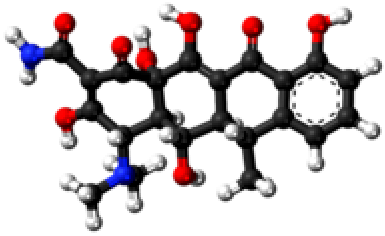
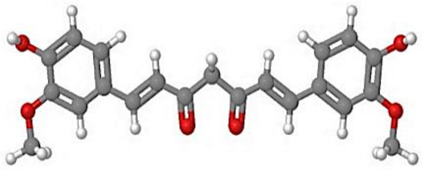
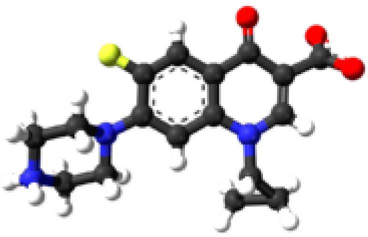
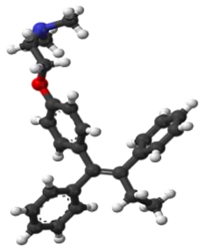
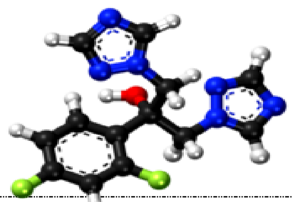
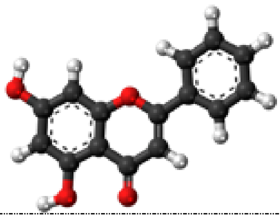
Gelatin nanofibers as potential anti-cancer drug delivery structures

In latest years, anticancer nanomedicines have mainly been progressed for chemotherapy and combination therapy in which the chief contributing anticancer drugs (Synthetic anti-cancer drugs like Curcumin (1, 38-40) and Herbal anti-cancer drugs like Doxorubicin (41, 42) are delivered by deliberately designed nano drug delivery systems (43-45). Table 1 presents the application of gelatin nano-mats as novel anti-cancer delivery systems.

Table 1. Novel gelatin nano-fibrous structure as anti-cancer delivery systems

Gelatin Nanomat		**Drug**	**Ref.**
Chemical Formulation	**Phisycal Structure**		
Gelatin+Polycaprolactone	Nanofibrous Mat	Lupeol ($C_{30}H_{50}O$)  	(46)
Gelatin+Poly(3-hydroxybutyric acid)	Nanofibrous Scaffold	Methotrexate ($C_{20}H_{22}N_8O_5$) 	(47)
Gelatin+Poly(l-lactide-co-ε-caprolactone)	Core-shell Nanofibers	Doxorubicin ($C_{27}H_{29}NO_{11}$) 	(48, 49)
Gelatin	Forcespun Nanofibers	Isorhamnetin ($C_{16}H_{12}O_7$)	(50)
Gelatin+Poly(caprolactone)	Nanofibers	5-Fluorouracil($C_4H_3FN_2O_2$)  	(51)

[DOI: 10.22088/crms.6.1.25]

Gelatin+Poly-caprolactone+ Hydroxyapatite nanoparticles	Hybrid Nanofibers	Doxycycline($C_{22}H_{24}N_2O_8$) 	(52)
Gelatin	Electrospun nanofibers	Curcumin($C_{21}H_{20}O_6$) 	(53), (54-
Gelatin+poly(lactide-co-ε-caprolactone)	Electrospun nanofibers	Ciprofloxacin($C_{17}H_{18}FN_3O_3$) 	(51)
Gelatin	Nanofibers	Tamoxifen($C_{26}H_{29}NO$) 	(56, 62)
Gelatin+Poly (vinyl alcohol)	Multilayer Nanofibers	Fluconazole ($C_{13}H_{12}F_2N_6O$) 	(63)
Gelatin+Poly(caprolactone)	Nanofibers	Chrysin($C_{15}H_{10}O_4$) 	(64)

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Conclusion

Gelatin has been shown to be a prospective biopolymer to be applied in drug delivery uses owing to its biocompatibility and bio degradability nature. In contrast nanofibers can be applied to deliver anti-cancer drugs, so as Gelatin nanofibers are the novel biomaterials which are capable as drug carriers in human body for numerous applications like cancer therapy. This mini-review gives detailed information about the recent developments and uses of gelatin nanofibers as anti-cancer drug delivery vehicles for cancer treatment.

Future aspects

The author proposes an alternative strategy “Ultraviolet/O3 surface treatment” on gelatin nanofibers (for reduction of hydrophobicity). This strategy is expected to increase the success of anticancer drug solution in the gelatin nano-mats.

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Competing Interests

The author declares no conflict of interest.

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